Quality Insurance of rectal cancer – phase 3: statistical methods to benchmark centers on a set of quality indicators – Supplement part II

KCE reports 161S

Belgian Health Care Knowledge Centre
Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
2011

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Federaal Kenniscentrum voor de gezondheidszorg - Centre fédéral d'expertise des soins de santé –
Belgian Health Care Knowlegde Centre.
Centre Administratif Botanique, Doorbuilding (10th floor)
Boulevard du Jardin Botanique 55
B-1000 Brussels
Belgium
Tel: +32 [0]2 287 33 88
Fax: +32 [0]2 287 33 85
Email : info@kce.fgov.be
Web : http://www.kce.fgov.be

Quality Assurance of rectal cancer diagnosis and treatment – phase 3: statistical methods to benchmark centres on a set of quality indicators – Supplement part II

KCE reports 161S

ELS GOETGHEBEUR, RONAN VAN ROSSEM, KATRIEN BAERT, KURT VANHOUTTE, TOM BOTERBERG, PIETER DEMETTER, MARK DE RIDDER, DAVID HARRINGTON, MARC PEETERS, GUY STORME, JOHANNA VERHULST, VLAYEN JOAN, VRIJENS FRANCE, STIJN VANSTEELANDT, WIM CEELEN.

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Title: Quality Insurance of rectal cancer – phase 3: statistical methods to benchmark centers on a set of quality indicators – Supplement part II

Authors: Els Goetghebeur (UGent), Ronan Van Rossem (UGent), Katrien Baert (UGent), Kurt Vanhoutte (UGent), Tom Boterberg (UZ Gent), Pieter Demetter (Erasme), Mark De Ridder (UZ Brussel), David Harrington (Harvard), Marc Peeters (UZ Antwerp), Guy Storme (UZ Brussel), Johanna Verhulst (UZGent), Joan Vlayen (KCE), France Vrijens (KCE), Stijn Vansteedlandt (Ugent), Wim Ceelen (UZgent)

Reviewers: none

External experts: PROCARE members: Anne Jouret-Mourin (UCL), Alex Kartheuser (UCL), Stephanie Laurent (UZGent), Gaëtan Molle (Hôpital Jolimont La Louvière), Freddy Penninckx (UZ Leuven, president steering group), Jean-Luc Van Laethem (ULB), Koen Vindevoghel (OLV Lourdes Waregem), Xavier de Béthune (ANMC), Catherine Legrand (UCL), Stefan Michiels (Institut Bordet), Ward Rommel (Vlaamse Liga tegen Kanker)

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External validators: Pr Johan Hellings (ICURO), Pr Pierre Honoré (CHU Liège), Pr Hans C. van Houwelingen (Leiden University).

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Appendix 5: Survey on the clinical importance and reliability of reporting of all QCIs discussed in the PROCARE consensus (July 2010)

INTRODUCTION

This document provides the updated list of quality of care indicators (QCIs) to be used for feedback to the centers, according to the PROCARE consensus of July 24th, 2010.

We kindly ask you to indicate, for each QCI, 1) how you judge the **clinical importance** of this QCI for evaluating rectal cancer care and 2) to what extent you think this QCI is **reported reliably** for each patient in the database.

Please cross out only one possible answer.

Additional thoughts or comments about specific QCIs, are invited in the "…" in the lower box.

As described in the main report of Deliverable 3 ("Dimensions of care and their aggregation") of this project, the results of this survey will play an important role in the selection of QCIs for constructing aggregate domain-specific and outcome- and process quality indicators (QIs).

Many thanks for your kind corporation.

1 GENERAL QUALITY INDICATORS

1.1 OVERALL 5-YEAR SURVIVAL BY STAGE (KCE 2008 QCI 1111; OUTCOME INDICATOR)

N: Number of patients in denominator that survived 1-5 years

D: Number of patients for whom the national registry number is known and have a follow-up of 1 -5 years, respectively. Survival status was obtained through cross-link with the Crossroads Bank for Social Security (CBSS).

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

1.2 DISEASE-SPECIFIC 5-YEAR SURVIVAL BY STAGE (KCE 2008 QCI 1112; OUTCOME INDICATOR)

The percentage of people in a study or treatment group who did not die from rectal cancer in a defined period of time. The time period begins at the incidence date. Date of incidence is defined by the date of pathological diagnosis (biopsy), if missing: by the date of first consultation or hospitalization, if still missing: by the date of first treatment (any type).

Patients who died without rectal cancer (LR or metastasis) are censored.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

1.3 RELATIVE SURVIVAL (NEW QCI 1112B; OUTCOME INDICATOR)

The relative survival is the ratio of observed survival in a population to the expected survival rate. It estimates the chance that a patient will survive a set number of years after a cancer diagnosis. It is calculated to exclude the chance of death from diseases other than the cancer and shows whether or not that specific disease shortens a person's life.

If reliable information on cause of death is available, it is preferable to use the 'adjusted rate', i.e. disease (rectal cancer)-specific survival. This is particularly true when the series is small or when the patients are largely drawn from a particular segment of the population (e.g. socioeconomic segment).

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

1.4 PROPORTION OF PATIENTS WITH LOCAL RECURRENCE (KCE 2008 QCI 1113; OUTCOME INDICATOR)

N: Number of patients in denominator who developed a local recurrence at 1-5 year

D: Number of (y)pStage 0-III patients with R0 resection who have a follow-up of 1-5 years, respectively.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

1.5 DISEASE-FREE SURVIVAL (NEW QCI 1113B; OUTCOME INDICATOR)

N: Number of patients in denominator who did not develop a local recurrence and/or distant metastasis at 1-5 year of follow-up.

D: Number of (y)pStage 0-III patients with R0 resection who have a follow-up of 1-5 years, respectively.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

2 DIAGNOSIS AND STAGING

2.1 PROPORTION OF PATIENTS WITH A DOCUMENTED DISTANCE FROM THE ANAL VERGE (KCE 2008 QCI 1211; PROCESS INDICATOR)

N: Number of patients in denominator for whom lower limit of the tumour is known (see definition lower limit of tumour)

D: Number of registered patients

Priority sequence to determine lower limit: 1. pretreatment rectoscopy, 2. pretreatment colonoscopy, 3. rectoscopy or colonoscopy at surgery.

Table 1: Level of tumour (lower limit determined by distance from anal verge)

Lower limit tumour (LL)	Level tumour
≤ 5 cm	Low
>5 - ≤ 10 cm	Mid
>10 cm	High

For patients with long course neoadjuvant radiotherapy the pretreatment lower limit is taken as lower limit of the tumour. If no lower limit is available before neoadjuvant treatment, the lower limit measured at surgery is taken as lower limit of the tumour.

For patients who received neoadjuvant treatment but for whom it is not known whether they received short or long course radiotherapy, the lowest limit of either the pretreatment or the lower limit at surgery is taken.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable

☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

2.2 PROPORTION OF PATIENTS IN WHOM A CT OF THE ABDOMEN AND RX OR CT THORAX WAS PERFORMED BEFORE ANY TREATMENT (KCE 2008 QCI 1212; PROCESS INDICATOR)

N: Number of patients in denominator in whom an abdominal CT and (rx thorax or CT thorax) was performed before any treatment

D: Number of registered patients with elective or scheduled surgery after August 1st 2008.

Until now not used for PROCARE feedback because the use of CT may be underestimated in patients registered using forms dating prior to August 1st 2008 (related to the structure and formulation of the early forms).

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

2.3 PROPORTION OF PATIENTS IN WHOM A CEA WAS PERFORMED BEFORE ANY TREATMENT (KCE 2008 QCI 1213; PROCESS INDICATOR)

N: Number of patients in denominator for whom CEA serum level before treatment is reported

D: Number of registered patients

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

2.4 PROPORTION OF PATIENTS UNDERGOING ELECTIVE SURGERY THAT HAD PREOPERATIVE COMPLETE LARGE BOWEL-IMAGING (KCE 2008 QCI 1214; PROCESS INDICATOR)

N: Number of patients in denominator who underwent a total coloscopy or a complete double contrast enema or virtual colonoscopy

D: Number of patients treated with elective or scheduled surgery.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important

- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable

- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

2.5 USE OF TRUS IN CT1/CT2 (NEW QCI 1214B; PROCESS INDICATOR)

N: Number of patients in denominator in whom cT was based on TRUS

D: Number of patients with cT1 or cT2 rectal cancer registered after August 1st 2008

CAUTION: the use of TRUS may be underestimated in patients registered using forms dating prior to August 1st 2008.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

2.6 USE OF MRI IN CSTAGE II OR III (NEW QCI 1214C; PROCESS INDICATOR)

N: Number of patients in denominator in whom cT was based on MRI

D: Number of patients with cStage II or III rectal cancer based on any imaging technique registered after August 1st 2008.

CAUTION: the use of MRI may be underestimated in patients registered using forms dating prior to August 1st 2008.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

2.7 PROPORTION OF PATIENTS IN WHOM A TRUS AND PELVIC CT AND/OR PELVIC MRI WAS PERFORMED BEFORE ANY TREATMENT (KCE QCI 1215; PROCESS INDICATOR)

N: Number of patients in whom cT or cN were based on TRUS and at least one of the two following:

- pelvic CT
- pelvic MRI

D: Number of registered patients with rectal cancer of any stage

CAUTION: may be underestimated in patients registered using forms dating prior to August 1st 2008.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

2.8 PROPORTION OF PATIENTS WITH CSTAGE II-III RC THAT HAVE A REPORTED CCRM (KCE QCI 1216; PROCESS INDICATOR)

N: Number of patients in denominator for whom cCRM is reported

D: Number of patients with cStage II-III treated with radical surgical resection.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

2.9 ACCURACY OF CM0 STAGING (NEW QCI 1216B; PROCESS INDICATOR)

N: Patients in denominator in whom no metastatic disease was diagnosed within 3months following the date of first treatment (any type).

D: All patients with cStage I-III and for whom a 1 year follow-up is available.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

2.10 TIME BETWEEN FIRST HISTOPATHOLOGIC DIAGNOSIS AND FIRST TREATMENT (KCE QCI 1217; PROCESS INDICATOR)

For the patients treated by surgery and/or radiotherapy and/or chemotherapy, the time interval in days is computed between the date of pathologic diagnosis, if available, otherwise the date of first contact/hospitalization, and the date of first treatment.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

For this QCI, what target should be reached for 'good practice'?

...

2.11 ACCURACY OF CT/CN STAGING IF NO OR SHORT RADIOTHERAPY (SEPARATELY PRESENTED IN 2 TABLES) (NEW QCI; PROCESS INDICATOR)

For patients who did not receive neoadjuvant long course radio(chemo)therapy, the (y)pT/(y)pN is shown related to the cT/cN for these patients.

D: All patients with TRUS/CT/MRI with no or short neoadjuvant radiotherapy (without long R(C)T) and for whom the pT and pN is known and for whom the cT and cN is known (excluding patients with c and/or pTx and/or c and/or pNx.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

3 NEOADJUVANT TREATMENT

Definition:

- Short course regimen are 5 x 5, 10 or 13 x 3 Gy (always without chemotherapy).
- Long course regimen are 25 or more x 1.8 Gy (with or without chemotherapy).

3.1 PROPORTION OF CSTAGE II-III PATIENTS THAT RECEIVED A NEOADJUVANT PELVIC RT (NEW QCI 1221; PROCESS INDICATOR)

For high rectal cancer (> 10 cm)

N: Number of patients in denominator who received neoadjuvant **R(C)T**

D: Number of patients in cStage II or III, treated with radical surgical resection with tumour in upper third

For mid rectal cancer (>5 - 10 cm)

N: Number of patients in denominator who received neoadjuvant **R(C)T**

D: Number of patients in cStage II or III, treated with radical surgical resection with tumour in middle third

For low rectal cancer (≤ 5 cm)

N: Number of patients in denominator who received neoadjuvant treatment

D: Number of patients in cStage II or III, treated with radical surgical resection with tumour in lower third

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable

☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don’t know / No opinion
Do you have any comments on this QCI? ...

3.2 PROPORTION OF PATIENTS WITH CCRM ≤ 2 MM ON MRI/CT THAT RECEIVED LONG COURSE NEOADJUVANT RADIO(CHEMO)THERAPY (NEW QCI 1221B; PROCESS INDICATOR)

N: Number of patients in denominator who received long course neoadjuvant radio(chemo)therapy

D: Number of patients treated with radical surgical resection and for whom cCRM is **≤** 2 mm

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

3.3 PROPORTION OF PATIENTS WITH CSTAGE I THAT RECEIVED NEOADJUVANT RADIO(CHEMO)THERAPY (NEW QCI 1221C; PROCESS INDICATOR)

For high rectal cancer (> 10 cm)

N: Number of patients in denominator who received neoadjuvant R(C)T

D: Number of patients in cStage I, treated with radical surgical resection with tumour in upper third

For mid rectal cancer (>5 - 10 cm)

N: Number of patients in denominator who received neoadjuvant R(C)T

D: Number of patients in cStage I, treated with radical surgical resection with tumour in middle third

For low rectal cancer (≤ 5 cm)

N: Number of patients in denominator who received neoadjuvant treatment

D: Number of patients in cStage I, treated with radical surgical resection with tumour in lower third

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI?...

3.4 PROPORTION OF CSTAGE II-III PATIENTS TREATED WITH NEOADJUVANT 5-FU BASED CHEMORADIATION, THAT RECEIVED A CONTINUOUS INFUSION OF 5-FU (KCE 2008 QCI 1224; PROCESS INDICATOR)

N: Number of patients in denominator that received a continuous infusion of 5-FU.

D: Number of patients with cStage II-III treated with radical surgical resection and long course pelvic chemoradiotherapy

Note Not used in PROCARE feedback until 2009 because not enough data. Solved retrospectively (at least partially by means of reminders in spring 2010). Also, alternative methods became available in the meantime (e.g. oral capecitabine).

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

3.5 PROPORTION OF CSTAGE II-III PATIENTS TREATED WITH A LONG COURSE OF PREOPERATIVE PELVIC RT OR CHEMORADIATION, THAT COMPLETED THIS NEOADJUVANT TREATMENT WITHIN THE PLANNED TIMING (KCE 2008 QCI 1225; PROCESS INDICATOR)

N: Number of patients in denominator for whom the radiotherapy treatment was not interrupted for more than five working days

D: Number of patients with cStage II-III who started with long course neoadjuvant radiotherapy which was followed by radical surgical resection.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

3.6 PROPORTION OF CSTAGE II-III PATIENTS TREATED WITH A LONG COURSE OF PREOPERATIVE PELVIC RT OR CHEMORADIATION, THAT WAS OPERATED 4 TO 12 WEEKS AFTER COMPLETION OF THE (CHEMO)RADIATION (KCE 2008 QCI 1226; PROCESS INDICATOR)

N: Number of patients in denominator that was operated 4 to 12 weeks after completion of the (chemo)radiotherapy

D: Number of patients with cStage II-III treated with long course neoadjuvant radiotherapy and for whom date of surgery and date of last irradiation are not missing

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

3.7 RATE OF ACUTE GRADE 4 RADIO(CHEMO)THERAPY-RELATED COMPLICATIONS (KCE 2008 QCI 1227; PROCESS INDICATOR)

N: Number of patients in denominator that were presented acute grade 4 complications during/up to 8 weeks after completion of neoadjuvant or adjuvant (chemo)radiotherapy (long or short).

D: Number of patients treated with neoadjuvant or adjuvant radiotherapy and for whom follow-up data (at least until 1 year) are available.

Note Not used in PROCARE feedback until 2009 because not enough data. Solved retrospectively (at least partially by means of reminders in spring 2010).

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

4 SURGERY

4.1 PROPORTION OF R0 RESECTIONS (KCE 2008 QCI 1231; OUTCOME INDICATOR)

Definitions:

- R0 status. Resections are classified as R0 if cM does not equal 'M1' and if type of resection at surgery is not 'R2' and if no one of the four criteria of R1 status are present.
- R1 status. Resections are classified as R1 if cM does not equal 'M1' and if type of resection at surgery is not 'R2' and if at least one of the following four conditions is present:
  - (y)pCRM < 1 mm
  - distal resection margin < 1 mm
  - rectum perforation as indicated by the surgeon
  - rectum perforation as indicated by the pathologist
- R2 status. Resections are classified as R2 if cM equals M1 and/or metastasis are discovered at surgery (and not completely resected). Thus, if the type of resection at surgery is reported to be 'R2' then R status equals 'R2'.
- R status is reported as missing if cM status is missing and/or if data on two or more of the following criteria are missing: tumor free status of the (y)pCRM, the tumor free status of the distal resection margin, rectum perforation as indicated by the surgeon or pathologist.

R0 resection

N: Number of patients in denominator with R0 resection

D: Number of patients treated with radical surgical resection and for whom R status is not missing

R1 resection

N: Number of patients in denominator with R1 resection

D: Number of patients treated with radical surgical resection and for whom R status is not missing

R2 resection

N: Number of patients in denominator with R status equal ‘R2’

D: Number of patients treated with radical surgical resection and for whom R status is not missing

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don’t know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don’t know / No opinion
Do you have any comments on this QCI? ...

4.2 PROPORTION OF APR AND HARTMANN'S PROCEDURE OR TOTAL EXCISION OF COLON AND RECTUM WITH DEFINITIVE ILEOSTOMY (KCE 2008 QCI 1232A; OUTCOME INDICATOR)

Global (QCI)

N: Number of patients in denominator in whom APER or Hartmann's procedure or total excision of colon and rectum with definitive ileostomy was performed

D: Number of patients treated with any type of resection for rectal cancer at any known level

For high rectal cancer (> 10 cm)

N: Number of patients in denominator in whom APER or Hartmann's procedure or total excision of colon and rectum with definitive ileostomy was performed

D: Number of patients treated with any type of resection for tumour in upper third

For mid rectal cancer (>5 - 10 cm)

N: Number of patients in denominator in whom APER or Hartmann's procedure or total excision of colon and rectum with definitive ileostomy was performed

D: Number of patients treated with any type of resection for tumour in middle third

For low rectal cancer (≤ 5 cm)

N: Number of patients in denominator in whom APR or Hartmann's procedure or total excision of colon and rectum with definitive ileostomy was performed

D: Number of patients treated with any type of resection for tumour in lower third

4.3 PROPORTION OF PATIENTS WITH STOMA 1 YEAR AFTER SPHINCTER-SPARING SURGERY (KCE 2008 QCI 1232B; OUTCOME INDICATOR)

N: Number of patients in denominator still having a stoma 1 year after surgery

D: Number of patients treated with TME (complete rectum resection (TME) + straight CAA, coloplasty, pouch, side-to-end CAA, total excision of colon and rectum with IPAA, or another specified type of reconstruction) with a primary (constructed at the time of SSO) or secondary (constructed after SSO) derivative stoma or dismantling of anastomosis still alive 1 year after surgery and for whom follow-up at 1 year or more is known.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

4.4 RATE OF PATIENTS WITH MAJOR LEAKAGE OF THE ANASTOMOSIS AFTER PME + SSO + RECONSTRUCTION (NEW QCI 1233A; OUTCOME INDICATOR)

N: Number of patients with major leakage of the anastomosis (requiring reoperation for leakage)

D: Number of patients treated with PME (high or low anterior resection with colorectal anastomsosis) and for whom it is reported whether there were postoperative complications or not.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

4.5 RATE OF PATIENTS WITH MAJOR LEAKAGE OF THE ANASTOMOSIS AFTER TME + SSO + RECONSTRUCTION (GLOBAL, I.E. WITH OR WITHOUT PRIMARY DERIVATIVE STOMA) (NEW QCI 1233B; OUTCOME INDICATOR)

N: Number of patients with major leakage of the anastomosis (requiring reoperation for leakage)

D: Number of patients treated with TME (complete rectum resection (TME) + straight CAA, coloplasty, pouch, side-to-end CAA, total excision of colon and rectum with IPAA, or another specified type of reconstruction) and for whom it is reported whether there were postoperative complications or not

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

4.6 INPATIENT OR 30-DAY MORTALITY (KCE 2008 QCI 1234; OUTCOME INDICATOR)

N: Number of patients in denominator who died in hospital or within 30 days after surgery

D: Number of patients treated with radical surgical resection and for whom it is known whether they died in hospital or within 30 days after surgery and for whom the dates of surgery and survival or death are known.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

4.7 POSTOPERATIVE MAJOR SURGICAL MORBIDITY WITH REINTERVENTION UNDER NARCOSIS AFTER RADICAL SURGICAL RESECTION (NEW QCI 1234B; OUTCOME INDICATOR)

N: Number of patients in denominator who presented major surgical morbidity requiring reintervention under narcosis

D: Number of patients treated with radical surgical resection and for whom postoperative data on morbidity/mortality are available

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

4.8 RATE OF INTRA-OPERATIVE RECTAL PERFORATION (KCE 2008 QCI 1235; OUTCOME INDICATOR)

N: Number of patients in denominator for whom the surgeon and/or pathologist reported rectal perforation

D: Number of patients treated with radical surgical resection and for whom perforation of the rectum (yes or no) is reported by either the surgeon or the pathologist.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

4.9 (Y)P DISTAL MARGIN INVOLVED (POSITIVE) AFTER SSO OR HARTMANN FOR LOW RECTAL CANCER (≤ 5 CM) (NEW QCI 1235B; OUTCOME INDICATOR)

N: Number of patients in denominator for whom the (y)p distal margin is invaded

D: Number of patients treated with Hartmann's procedure or SSO for rectal cancer in the lower third and for whom it is reported whether the (y)p distal margin is free or invaded.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

4.10 MESORECTAL (Y)PCRM POSITIVITY AFTER RADICAL SURGICAL RESECTION (NEW QCI 1235C; OUTCOME INDICATOR)

Note The definition of positivity (≤ 1 mm) differs with the definition of R1 status (invaded). It should apply only to the lateral margin of the mesorectum not to serosal positivity

Global

N: Number of patients in denominator for whom the mesorectal (y)pCRM ≤ 1 mm

D: Number of patients treated with radical surgical resection and for whom the mesorectal (y)pCRM is known

For high rectal cancer (> 10 cm)

N: Number of patients in denominator for whom the mesorectal (y)pCRM ≤ 1 mm

D: Number of patients treated with radical surgical resection with tumour in highest third and for whom (y)pCRM is known

For mid rectal cancer (>5 - 10 cm)

N: Number of patients in denominator for whom the mesorectal (y)pCRM ≤ 1 mm

D: Number of patients treated with radical surgical resection with tumour in middle third and for whom (y)pCRM is known

For low rectal cancer (≤ 5 cm)

N: Number of patients in denominator for whom the mesorectal (y)pCRM ≤ 1 mm

D: Number of patients treated with radical surgical resection with tumour in lowest third and for whom the mesorectal (y)pCRM is known

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database?

☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don’t know / No opinion
Do you have any comments on this QCI? ...

5 ADJUVANT TREATMENT

5.1 PROPORTION OF (Y)PSTAGE III PATIENTS WITH R0 RESECTION THAT RECEIVED ADJUVANT CHEMOTHERAPY WITHIN 3 MONTHS AFTER SURGERY (KCE 2008 QCI 1241; PROCESS INDICATOR)

N: Number of patients in denominator receiving adjuvant chemotherapy within 3 months after surgery

D: Number of patients treated with R0 radical surgical resection for (y)pStage III and for whom it is known whether they received adjuvant chemotherapy within 6 months after surgery or not.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

5.2 PROPORTION OF PSTAGE II-III PATIENTS WITH R0 RESECTION THAT RECEIVED ADJUVANT RADIOTHERAPY OR CHEMORADIOTHERAPY WITHIN 3 MONTHS AFTER SURGERY (KCE 2008 QCI 1242; PROCESS INDICATOR)

N: Number of patients in denominator receiving adjuvant radio(chemo)therapy within 3 months after surgery

D: Number of patients treated with R0 radical surgical resection for pStage II or III without neoadjuvant treatment and for whom it is known whether they received adjuvant radio(chemo)therapy or not.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

5.3 PROPORTION OF (Y)PSTAGE II-III PATIENTS WITH R0 RESECTION THAT STARTED ADJUVANT CHEMOTHERAPY WITHIN 12 WEEKS AFTER SURGICAL RESECTION (KCE 2008 QCI 1243; PROCESS INDICATOR)

N: Number of patients in denominator receiving adjuvant chemotherapy within 3 months after surgery

D: Number of patients treated with R0 radical surgical resection for (y)pStage II or III and for whom it is known whether they received adjuvant chemotherapy or not.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

5.4 PROPORTION OF (Y)PSTAGE II-III PATIENTS WITH R0 RESECTION TREATED WITH ADJUVANT CHEMO(RADIO)THERAPY, THAT RECEIVED 5-FU BASED CHEMOTHERAPY (KCE 2008 QCI 1244; PROCESS INDICATOR)

N: Number of patients in denominator receiving 5-fluorouracil based adjuvant chemotherapy

D: Number of patients who received adjuvant (radio)chemotherapy within 3 months after R0 radical surgical resection for (y)pStage II or III and for whom the type of adjuvant chemotherapy is known.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

5.5 RATE OF ACUTE GRADE 4 CHEMOTHERAPY-RELATED COMPLICATIONS (KCE 2008 QCI 1245; PROCESS INDICATOR)

N: Number of patients in denominator that presented acute grade 4 complications during or within 4 weeks after completion of adjuvant chemo(radio)therapy

D: Number of patients treated with adjuvant chemotherapy and for whom follow-up data (at least until 1 year) are available.

Note Not used in PROCARE feedback until 2009 because not enough data. Solved retrospectively (at least partially by means of reminders in spring 2010).

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

6 PALLIATIVE TREATMENT

6.1 RATE OF CSTAGE IV PATIENTS RECEIVING CHEMOTHERAPY (KCE 2008 QCI 1251; PROCESS INDICATOR)

N: Number of patients in denominator that received chemotherapy

D: Number of patients with cStage IV and for whom it is known whether they received chemotherapy or not.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

7 FOLLOW-UP

7.1 RATE OF CURATIVELY TREATED PATIENTS THAT RECEIVED A COLONOSCOPY WITHIN 1 YEAR AFTER RESECTION (KCE 2008 QCI 1261; PROCESS INDICATOR)

N: Number of patients in denominator that received a colonoscopy

D: Number of patients treated with curative resection for c(p)Stage I-III and for whom follow-up data (at least until 2 years) are available.

Note Not used in PROCARE feedback until 2009 because not enough data. Solved retrospectively (at least partially by means of reminders in spring 2010).

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

7.2 LATE GRADE 4 COMPLICATIONS OF RADIOTHERAPY OR CHEMORADIATION (KCE 2008 QCI 1263; PROCESS INDICATOR)

N: Number of patients in denominator that presented late grade 4 complications after completion of (neo)adjuvant chemo(radio)therapy

D: Number of patients treated with neoadjuvant or adjuvant radio(chemo)therapy and for whom follow-up data (at least until 1 year) are available.

Note Not used in PROCARE feedback until 2009 because not enough data.

Grade refers to the severity of the AE. The CTCAE v3.0 displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline: Grade 1: Mild AE, Grade 2: Moderate AE, Grade 3: Severe AE, Grade 4: Life-threatening or disabling AE (An AE whose existence or immediate sequelae are associated with an imminent risk of death) and Grade 5: Death related to AE.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

8 HISTOPATHOLOGIC EXAMINATION

8.1 USE OF THE PATHOLOGY REPORT SHEET (KCE 2008 QCI 1271; PROCESS INDICATOR)

N: Number of patients in denominator for whom a pathology report sheet was completed

D: Number of patients treated with (local or radical) resection and for whom date of resection is later than or equal to the 1st of January 2007.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care?

- ☐ Most important
- ☐ Very important
- ☐ Important
- ☐ Less important
- ☐ Not important
- ☐ Don't know / No opinion

To what extent do you think this QCI **is reported reliably** for each patient in the database?

- ☐ Most reliable
- ☐ Very reliable
- ☐ Reliable
- ☐ Less reliable
- ☐ Not reliable
- ☐ Don't know / No opinion

Do you have any comments on this QCI?

...

8.2 QUALITY OF TME ASSESSED ACCORDING TO QUIRKE AND MENTIONED IN THE PATHOLOGY REPORT (KCE 2008 QCI 1272; PROCESS INDICATOR)

N: Number of patients for whom the external surface of TME was reported in the pathology report sheet

D: Number of patients treated with TME as indicated by the surgeon after the 1st of January 2007.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

8.3 DISTAL TUMOUR-FREE MARGIN MENTIONED IN THE PATHOLOGY REPORT (KCE 2008 QCI 1273; PROCESS INDICATOR)

N: Number of patients in denominator for whom the length of the distal free tumour free margin was reported in the pathology report

D: Number of patients treated with SSO or Hartmann's procedure.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

8.4 DISTAL MARGIN INVOLVEMENT MENTIONED AFTER SSO OR HARTMANN (NEW QCI 1273B, PARTIALLY REPLACING KCE QCI 1231; OUTCOME QCI)

N: Number of patients in denominator for whom it was reported whether the distal resection margin was invaded

D: Number of patients treated with Hartmann's procedure or SSO with reconstruction and for whom a pathology report sheet was completed.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

8.5 NUMBER OF LYMPH NODES EXAMINED (KCE 2008 QCI 1274; PROCESS INDICATOR)

The median number of lymph nodes examined is computed for the following conditions:

- no or short course neoadjuvant RT
- long course neoadjuvant RT
- course type missing

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...
For this QCI, what target should be reached for 'good practice'? ...

8.6 (Y)PCRM MENTIONED IN MM IN THE PATHOLOGY REPORT (KCE 2008 QCI 1275; PROCESS INDICATOR)

N: Number of patients in denominator for whom the mesorectal (y)pCRM was mentioned in the pathology report

D: Number of patients treated with radical surgical resection and for whom a pathology report was completed.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

8.7 TUMOUR REGRESSION GRADE MENTIONED IN THE PATHOLOGY REPORT (AFTER NEOADJUVANT TREATMENT) (KCE 2008 QCI 1276; PROCESS INDICATOR)

N: Number of patients in denominator having their tumour regression grade mentioned in the pathology report

D: Number of patients treated with neoadjuvant long course radio(chemo)therapy and surgery.

How do you judge the **clinical importance** of this QCI for evaluating rectal cancer care? ☐ Most important ☐ Very important ☐ Important ☐ Less important ☐ Not important ☐ Don't know / No opinion
To what extent do you think this QCI **is reported reliably** for each patient in the database? ☐ Most reliable ☐ Very reliable ☐ Reliable ☐ Less reliable ☐ Not reliable ☐ Don't know / No opinion
Do you have any comments on this QCI? ...

Appendix 6: Descriptives of the prognostic factors and QCIs and detailed results of analysis of individual QCIs

TABLE OF CONTENT

FOREWORD

In this Appendix 6, we apply the first set of methods to the data available in the PROCARE register up to August 27th, 2010. We embark on a multivariate risk adjustment of outcome QCIs and univariate risk adjustments for process QCIs in all 8 domains.

Section 1 contains a list of descriptive tables and figures, for both prognostic factors and individual QCI's. Results per center are shown in caterpillar plots and outlying centers on either side of the spectrum are noted.

Section 2 is a detailed analysis of all QCI's in the PROCARE database (often with reference to descriptives and caterpillar plots in section 1).

Since the data register is in constant development and not yet fully matured, results should be interpreted with caution. In particular, certain variables show more missing data than one would normally expect, others still show some inconsistencies and for specific survival outcomes, few events result in a very weak information base and instability of the statistical methods used. Correspondingly, the implementation developed below serves first and foremost as an illustration of the application of the methods in this setting, for now adapted to the early version of the database.

NOTATION

QCI	Abbreviations	Description
1111	OS	Overall survival
1112	DSS	Disease-specific survival
1112b	RS	Relative survival
1113	LRFS	Proportion of patients with local recurrence
1113b	DFS	Disease-free survival
1211	%DocDist	Proportion of patients with a documented distance from the anal verge
1212	%CT_Preop	Proportion of patients in whom a CT of the abdomen and RX or CT thorax was performed before any treatment
1213	%CEA_Preop	Proportion of patients in whom a CEA was performed before any treatment
1214	%Preop_Bowel_Im	Proportion of patients undergoing elective surgery that had preoperative complete large bowel-imaging
1214b	%TRUS_cT12	Use of TRUS in cT1/cT2
1214c	%MR_cII/III	Use of MRI in cStage II or III
1215	%Preop_Im	Proportion of patients in whom a TRUS and pelvic CT and/or pelvic MRI was performed before any treatment
1216	%cCRM_rep	Proportion of patients with cStage II-III RC that have a reported cCRM
1216b	cM0_Acc	Accuracy of cM0 staging
1217	Time_histo-1ther	Time between first histopathologic diagnosis and first treatment
1221	%Preop_RT	Proportion of cStage II-III patients that received a

		neoadjuvant pelvic RT
1221b	%(C)RT_cCRM+	Proportion of patients with cCRM = 2 mm on MRI/CT that received long course neoadjuvant radio(chemo)therapy
1221c	%Preop_RT_cI	Proportion of patients with cStage I that received neoadjuvant radio(chemo)therapy
1224	%Preop_cont_5FU	Proportion of cStage II-III patients treated with neoadjuvant 5-FU based chemoradiation that received a continuous infusion of 5-FU
1225	%Completed_preop_RT	Proportion of cStage II-III patients treated with a long course of preoperative pelvic RT or chemoradiation that completed this neoadjuvant treatment within the planned timing
1226	%Surg<12w_after_Preop_RT	Proportion of cStage II-III patients treated with a long course of preoperative pelvic RT or chemoradiation that was operated 4 to 12 weeks after completion of the (chemo)radiation
1227	%grade4_Tox_Preop_RT	Rate of acute grade 4 radio(chemo)therapy-related complications
1231	%R0res	Proportion of R0 resections
1232a	%Defin_ostomy	Proportion of APR- Hartmann's procedure or total excision of colon and rectum with definitive ileostomy
1232b	%stoma1year	Proportion of patients with stoma 1 year after sphincter-sparing surgery
1233a	%Leak_PME	Major leakage after PME + SSO + reconstruction
1233b	%Leak_TME	Major leakage after TME + SSO + reconstruction (global)
1234	30d_mort	Inpatient or 30-day mortality after radical surgical resection
1234b	%Major_morb	Postoperative major surgical morbidity with reintervention under narcosis after radical surgical resection
1235	%Perfor	Rate of intra-operative rectal perforation
1235b	%Pos_Dist_margin	(y)p Distal margin involved (positive) after SSO or Hartmann for low rectal cancer (= 5 cm)
1235c	%Pos_CRM	Mesorectal (y)pCRM positivity after radical surgical resection
1241	%Adj-Chemo<3m	Proportion of (y)pStage III patients with R0 resection that received adjuvant chemotherapy within 3 months after surgery
1242	%Adj_RT<3m	Proportion of pStage II-III patients with R0 resection that received adjuvant radiotherapy or chemoradiotherapy within 3 months after surgery
1243	%Adj_Chemo<12w	Proportion of (y)pStage II-III patients with R0 resection that started adjuvant chemotherapy within 12 weeks after surgical resection
1244	%Adj_5FU	Proportion of (y)pStage II-III patients with R0 resection treated with adjuvant chemo(radio)therapy that received 5-FU based chemotherapy
1245	%grade4_Tox_Prostop_CT	Rate of acute grade 4 chemotherapy-related complications
1251	%cStage4_Chemo	Rate of cStage IV patients receiving chemotherapy
1261		Rate of curatively treated patients that received a colonoscopy within 1 year after resection
1263	%Late_Tox_RT	Late grade 4 complications of radiotherapy or chemoradiation
1271	%Path_Rep_Use	Use of the pathology report sheet
1272	%TME_Qual_Rep	Quality of TME assessed according to Quirke and mentioned in the pathology report
1273	%Dist_Margin_Pos_Rep	Distal margin involvement mentioned after SSO or Hartmann
1273b	%Dist_Margin_Rep	Distal tumour-free margin mentioned in the pathology report
1274	#Nodes_Examined	Number of lymph nodes examined
1275	pCRM_mm_Rep	(y)pCRM mentioned in mm in the pathology report
1276	TRG_Rep	Tumour regression grade mentioned in the pathology report (after neoadjuvant treatment)

Abbreviations:

ARP: abdominoperineal;

ASA: *American Society of Anesthesiologists*;

cCRM: *clinically assessed tumor-free circumferential resection margin*;

CT: *computed tomography;*

cN: *nodal status*;

cT: *clinical tumor*;

CEA: carcinoembryonic antigen (test);

MRI: *Magnetic Resonance Imaging*;

PME: *high or low anterior resection with colorectal anastomosis*;

PROCARE: *project on cancer of the rectum*;

QCI: *quality of care indicator*; R0 resection: *margin negative resection*;

SSO: *sphincter-saving operation*;

TME: *complete rectum resection*;

TNM: *Tumour Node Metastasis (cancer staging method; T describes the tumor, N describes the lymph nodes, and M describes distant metastasis; clinical stage and pathologic stage are denoted by a small "c" or "p" before the stage)*;

TRUS: *transrectal ultra sound*; (y)p

CRM: *pathologic tumor-free circumferential resection margin either with (ypCRM) preoperative radio(chemo)therapy or without (pCRM) preoperative treatment;* 5-FU: *5-fluorouracil*

DESCRIPTIVES

1.1 PROGNOSTIC FACTORS

Notes

As of Figure 2, centers with less than 5 patients available for the analysis are presented as one.

The first three columns of all Tables in this Section contain the following information:

- Center: total and size-grouped centers,
- Total N: the total number of patients in the PROCARE database, and
- N (%): the number (percentage) of patients for which information on the variable of interest is available in the PROCARE database.

'SD' stands for standard deviation.

Figure 1: Occurrence of incidence dates over time. Each line represents a centre present in the database. Centers with less than 10 registered patients are indicated in red circles, centers with 10 or more patients are indicated in blue dots.

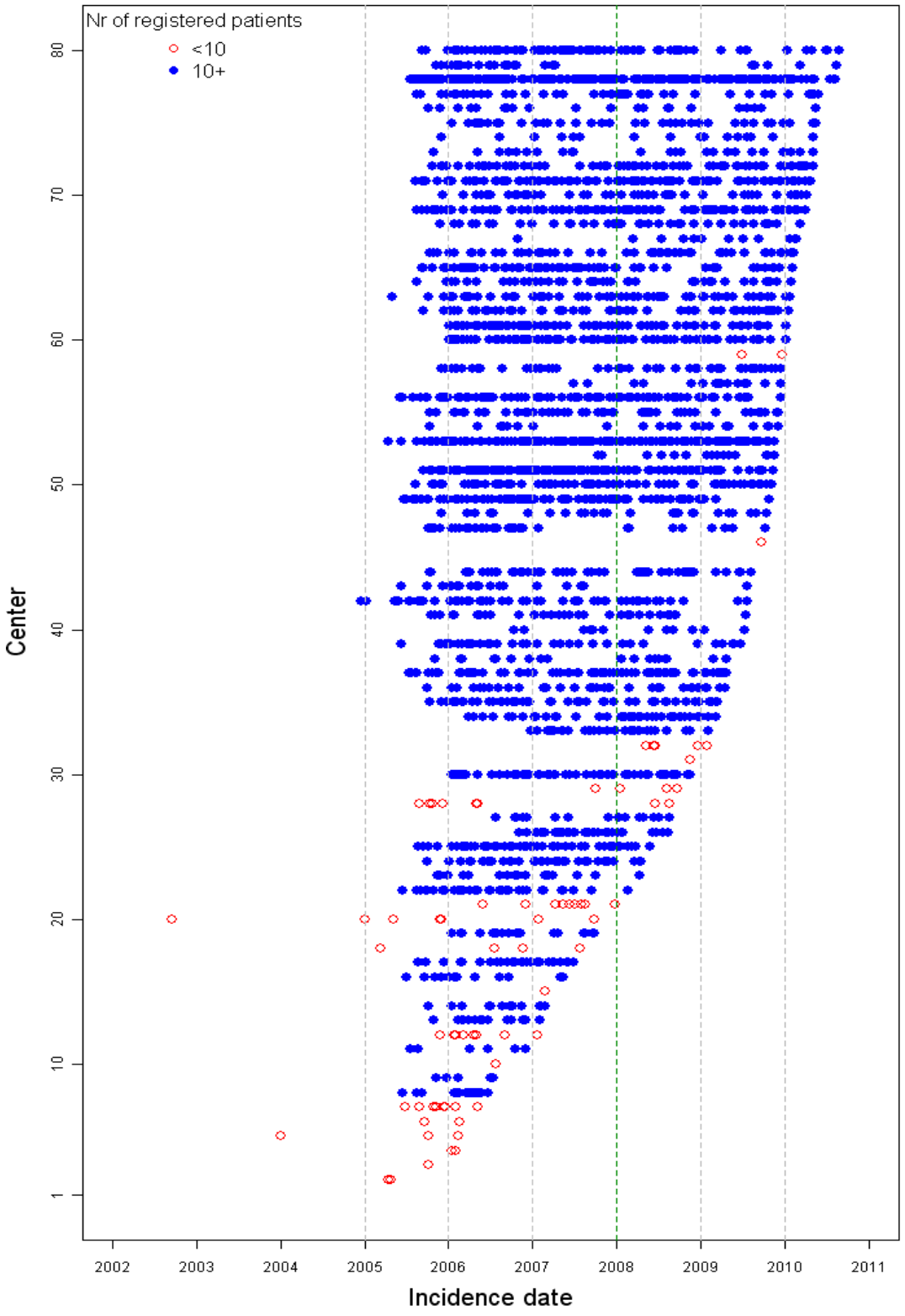


Table 1: Percentages of male patients for the size-grouped centers.

Center	Total N	N (%)	% Male
TOTAL	3328	3328 (100%)	61.4
[1-10[	68	68 (100%)	58.8
[10-20[	219	219 (100%)	65.3
[20-40[	424	424 (100%)	60.1
[40-60[	663	663 (100%)	59.1
[60-80[	399	399 (100%)	61.2
[80-100[	527	527 (100%)	58.3
[100-]	1028	1028 (100%)	64.6

Figure 2: Percentage male in individual centers, sorted by this percentage. Dots indicate mean values, bars indicate asymptotic 95% confidence intervals.

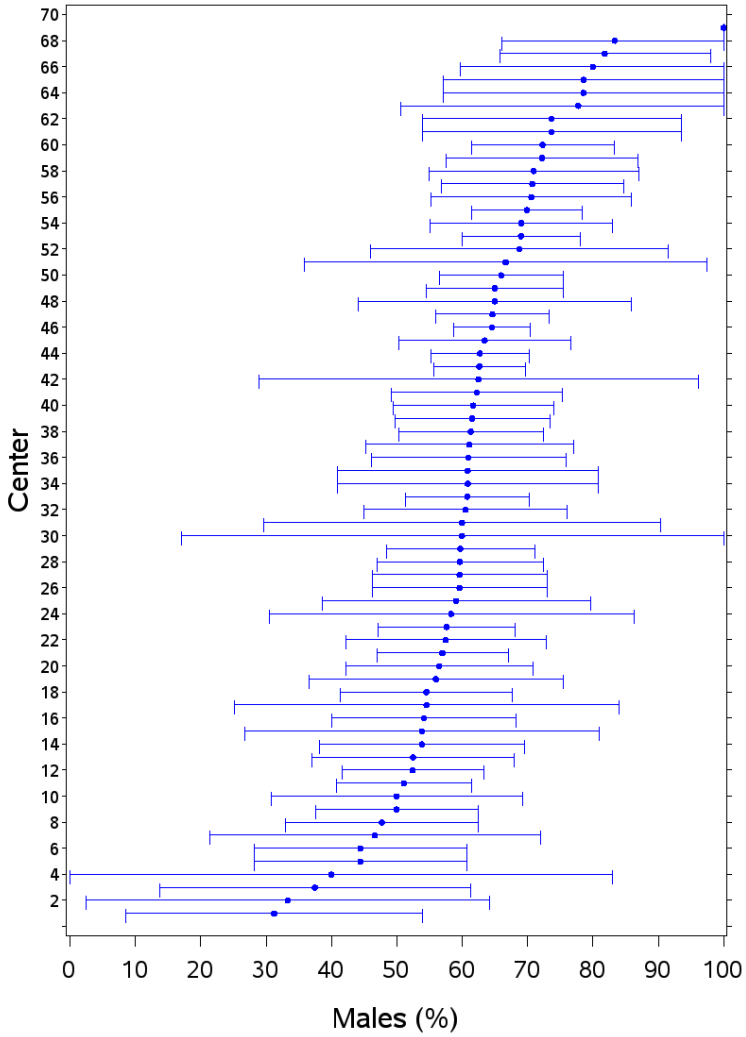


Table 2: Summary statistics for age, for size-grouped centers. The column '≥ 70' is the % of patients 70 years or older.

Center	Total N	N (%)	Min	P25	P50	P75	Max	Mean	SD	% ≥ 70
TOTAL	3328	3130 (94%)	21.00	60.00	68.00	76.00	95.00	67.22	11.83	46.4
[1-10[	68	66 (97%)	44.00	57.00	68.00	73.00	85.00	66.02	10.83	42.4
[10-20[	219	186 (85%)	35.00	60.00	68.00	76.00	89.00	67.63	11.51	46.2
[20-40[	424	409 (96%)	37.00	61.00	69.00	76.00	89.00	68.00	11.26	48.7
[40-60[	663	634 (96%)	35.00	61.00	70.00	77.00	93.00	68.62	11.29	51.1
[60-80[	399	353 (88%)	21.00	61.00	70.00	77.00	91.00	68.40	11.79	51.3
[80-100[	527	486 (92%)	30.00	61.00	69.00	77.00	94.00	68.42	11.59	49.0
[100-]	1028	996 (97%)	21.00	57.00	66.00	74.00	95.00	65.01	12.36	39.9

Figure 3: Box plots of age in individual centers, sorted by median age ('-' = median; '+' = mean; '□' = outlying observation).

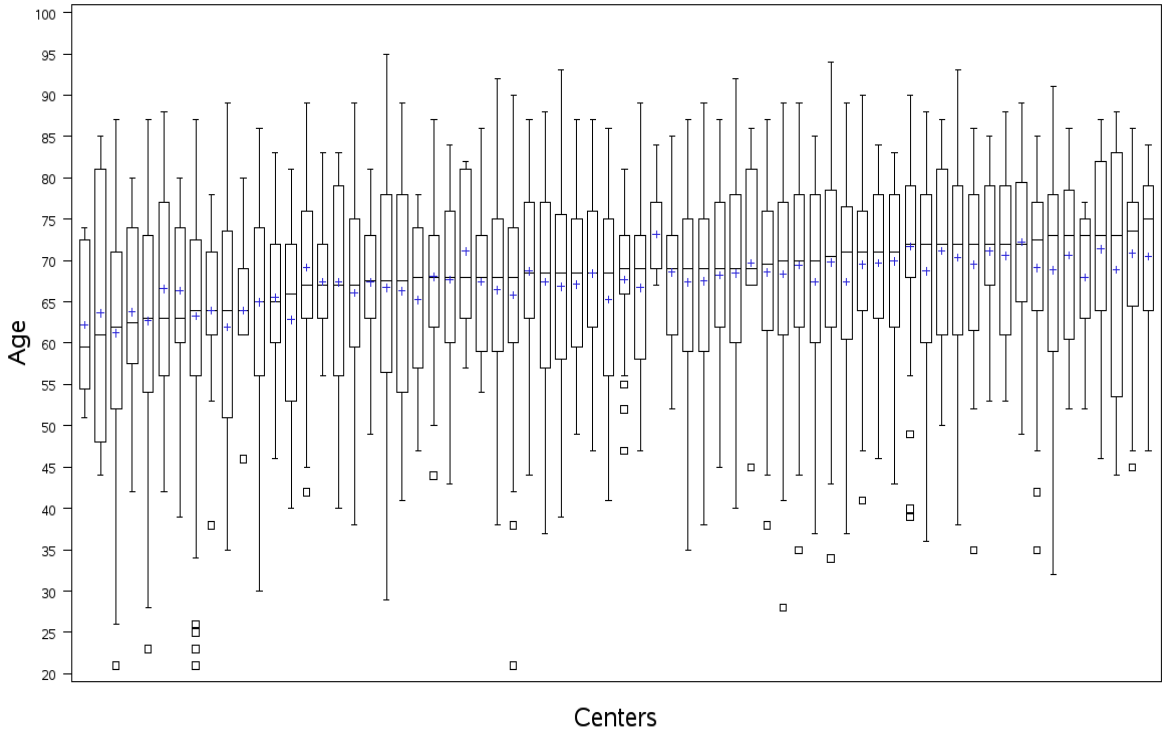


Table 3: Distribution (%) of cStage over size-grouped centers.

Center	Total N	N (%)	% 0	% I	% II	% III	% IV	% X	% missing
TOTAL	3328	3328 (100%)	0.3	11.8	14.8	45.7	12.6	3.1	11.8
[1-10[	68	68 (100%)	0.0	7.4	13.2	47.1	11.8	2.9	17.6
[10-20[	219	219 (100%)	0.5	9.6	20.1	37.4	13.2	2.3	16.9
[20-40[	424	424 (100%)	0.5	11.6	15.6	39.6	16.7	3.5	12.5
[40-60[	663	663 (100%)	0.0	11.8	17.3	40.3	12.4	4.8	13.4
[60-80[	399	399 (100%)	0.0	8.8	18.5	42.4	9.5	3.0	17.8
[80-100[	527	527 (100%)	0.8	13.9	13.5	43.1	12.1	3.2	13.5
[100-]	1028	1028 (100%)	0.3	12.7	11.0	55.9	12.4	1.9	5.7

Table 4: Distribution (%) of (y)pStage over size-grouped centers.

Center	Total N	N (%)	% 0	% I	%II	% III	% IV	% X	% missing
TOTAL	3328	3328 (100%)	7.6	20.9	21.3	22.4	13.9	5.3	8.5
[1-10[	68	68 (100%)	5.9	22.1	25.0	25.0	11.8	4.4	5.9
[10-20[	219	219 (100%)	3.2	16.0	21.9	17.8	14.6	11.4	15.1
[20-40[	424	424 (100%)	5.9	21.0	21.7	24.5	17.5	2.4	7.1
[40-60[	663	663 (100%)	6.2	20.8	25.0	19.6	13.6	4.1	10.7
[60-80[	399	399 (100%)	4.5	20.8	21.8	26.6	10.8	11.5	4.0
[80-100[	527	527 (100%)	7.8	17.5	19.2	20.7	13.7	5.5	15.7
[100-]	1028	1028 (100%)	11.5	23.8	19.3	23.3	13.8	3.7	4.6

Table 5: Distribution (%) of the three tumor levels over size-grouped centers.

Center	Total N	N (%)	% Low	% Mid	% High
TOTAL	3328	2838 (85%)	42.4	39.8	17.9
[1-10[	68	57 (84%)	50.9	40.4	8.8
[10-20[	219	167 (76%)	36.5	38.9	24.6
[20-40[	424	368 (87%)	39.9	41.3	18.8
[40-60[	663	564 (85%)	38.5	41.1	20.4
[60-80[	399	322 (81%)	42.9	41.3	15.8
[80-100[	527	457 (87%)	40.5	40.9	18.6
[100-]	1028	903 (88%)	47.1	37.3	15.6

Table 6: Summary statistics for BMI, for size-grouped centers.

Center	Total N	N (%)	Min	P25	P50	P75	Max	Mean (SD)
TOTAL	3328	2084 (63%)	12.89	22.72	25.16	28.05	58.77	25.74 (4.77)
[1-10[	68	45 (66%)	16.60	22.65	25.69	27.77	42.98	25.31 (4.79)
[10-20[	219	111 (51%)	18.94	22.72	25.22	29.32	58.68	26.98 (6.17)
[20-40[	424	274 (65%)	14.57	23.59	25.58	28.89	48.92	26.41 (4.85)
[40-60[	663	385 (58%)	16.02	22.77	25.15	28.30	52.07	25.81 (4.78)
[60-80[	399	211 (53%)	13.87	22.65	25.14	28.39	38.05	25.73 (4.51)
[80-100[	527	263 (50%)	12.89	22.48	25.31	28.00	58.77	25.56 (5.26)
[100-]	1028	795 (77%)	14.79	22.65	24.93	27.68	57.46	25.40 (4.36)

Center	Total N	N (%)	%Underweight BMI < 18.5	% Normal BMI < 30	% Obese 30 <= BMI < 35	% Morb obese BMI >= 35
TOTAL	3328	2084 (63%)	3.4	84.5	11.9	3.6
[1-10[	68	45 (66%)	6.7	88.9	8.9	2.2
[10-20[	219	111 (51%)	0.0	75.7	13.5	10.8
[20-40[	424	274 (65%)	1.5	82.1	12.8	5.1
[40-60[	663	385 (58%)	2.3	83.9	12.5	3.6
[60-80[	399	211 (53%)	5.2	83.9	12.8	3.3
[80-100[	527	263 (50%)	4.9	85.2	12.5	2.3
[100-]	1028	795 (77%)	3.8	86.5	10.9	2.5

Figure 4: Box plots of BMI in individual centers, sorted by median BMI ('-' = median; '+' = mean; '□' = outlying observation).

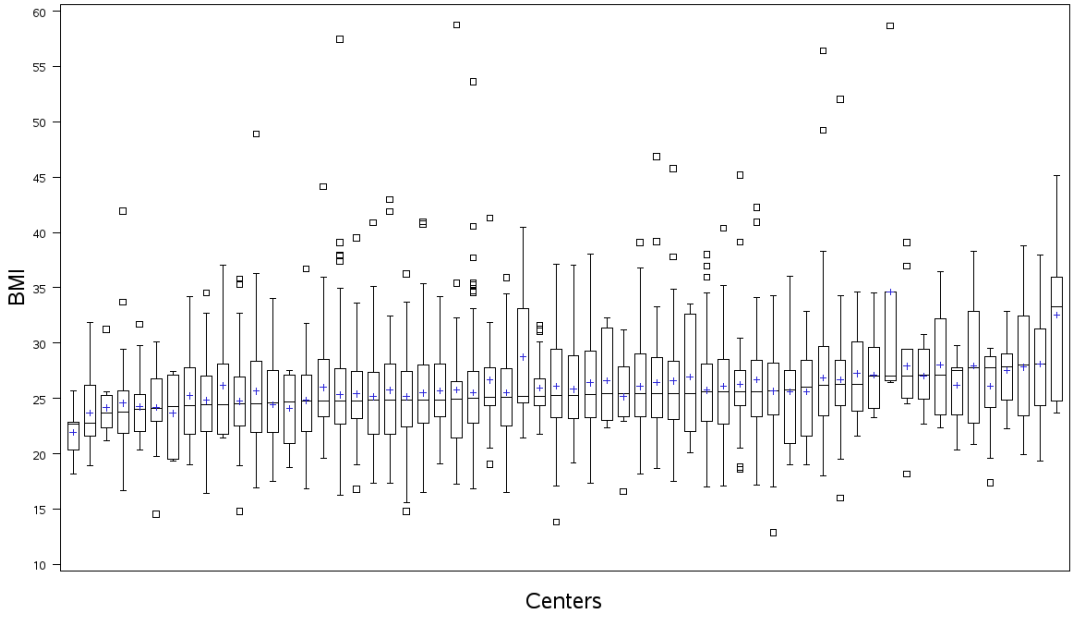


Table 7: Summary statistics for the ASA co-morbidity score, for size-grouped centers.

Center	Total N	N (%)	% I	% II	% III
TOTAL	3328	2637 (79%)	28.1	50.2	21.6
[1-10[	68	52 (76%)	19.2	55.8	25.0
[10-20[	219	169 (77%)	33.1	49.1	17.8
[20-40[	424	340 (80%)	32.6	45.9	21.5
[40-60[	663	496 (75%)	40.5	41.3	18.1
[60-80[	399	298 (75%)	24.5	46.3	29.2
[80-100[	527	396 (75%)	27.5	54.0	18.4
[100-]	1028	886 (86%)	20.5	56.4	23.0

Table 8: Percentages of patients with reported preoperative tumor complications, for size-grouped centers.

Center	Total N	N (%)	% tumor complications
TOTAL	3328	2948 (89%)	1.3
[1-10[	68	64 (94%)	0.0
[10-20[	219	173 (79%)	1.2
[20-40[	424	399 (94%)	1.3
[40-60[	663	594 (90%)	1.3
[60-80[	399	329 (82%)	0.6
[80-100[	527	456 (87%)	0.4
[100-]	1028	933 (91%)	2.0

Table 9: Percentages of patients for whom it is known that CEA was performed, for size-grouped centers.

Center	Total N	N (%)	% CEA
TOTAL	3328	3328 (100%)	81.3
[1-10[	68	68 (100%)	89.7
[10-20[	219	219 (100%)	75.3
[20-40[	424	424 (100%)	84.0
[40-60[	663	663 (100%)	79.8
[60-80[	399	399 (100%)	67.7
[80-100[	527	527 (100%)	77.8
[100-]	1028	1028 (100%)	89.0

Table 10: Distribution (%) of the different modes of surgery, for size-grouped centers.

Center	Total N	N (%)	% Elective / Scheduled	% Urgent / Emergency	% Missing

Center	Total N	N (%)	% Elective / Scheduled	% Urgent / Emergency	% Missing
TOTAL	3328	3328 (100%)	84.7	1.6	13.7
[1-10[	68	68 (100%)	85.3	2.9	11.8
[10-20[	219	219 (100%)	78.5	0.9	20.5
[20-40[	424	424 (100%)	85.6	3.3	11.1
[40-60[	663	663 (100%)	86.1	1.7	12.2
[60-80[	399	399 (100%)	83.5	1.5	15.0
[80-100[	527	527 (100%)	78.7	2.1	19.2
[100-]	1028	1028 (100%)	88.3	0.6	11.1

Table 11: Percentages of patients for whom it is known that they have a ventral tumor, for size-grouped centers

Center	Total N	N (%)	% Ventral tumor
TOTAL	3328	2494 (75%)	31.2
[1-10[	68	55 (81%)	29.1
[10-20[	219	141 (64%)	31.9
[20-40[	424	336 (79%)	32.7
[40-60[	663	493 (74%)	24.9
[60-80[	399	290 (73%)	26.9
[80-100[	527	391 (74%)	30.7
[100-]	1028	788 (77%)	36.4

Table 12: Percentages of patients for whom the cCRM is positive, for size-grouped centers

Center	Total N	N (%)	% Positive cCRM
TOTAL	3328	612 (18%)	73.2
[1-10[	68	4 (6%)	100.0
[10-20[	219	27 (12%)	77.8
[20-40[	424	52 (12%)	61.5
[40-60[	663	86 (13%)	73.3
[60-80[	399	37 (9%)	70.3
[80-100[	527	143 (27%)	70.6
[100-]	1028	263 (26%)	76.4

Table 13: Percentages of patients for whom the (y)pCRM is positive, for size-grouped centers

Center	Total N	N (%)	% Positive (y)pCRM
TOTAL	3328	2144 (64%)	18.1
[1-10[	68	46 (68%)	21.7
[10-20[	219	120 (55%)	16.7
[20-40[	424	273 (64%)	20.9
[40-60[	663	391 (59%)	18.4
[60-80[	399	292 (73%)	21.6
[80-100[	527	344 (65%)	14.5
[100-]	1028	678 (66%)	17.0

Table 14: Joint missingness patterns for prognostic factors.

N patients	Gender	Age	Tumor level	(y)pStage	cStage	ASA score	BMI	N missing
1722	1	1	1	1	1	1	1	0
84	1	1	1	1	1	0	1	1
126	1	1	1	1	0	1	1	1
66	1	1	1	0	1	1	1	1
499	1	1	1	1	1	1	0	1
39	1	1	0	1	1	1	1	1
6	1	1	1	1	0	0	1	2
3	1	1	1	0	1	0	1	2
21	1	1	1	0	0	1	1	2
2	1	0	1	1	1	1	0	2
214	1	1	1	1	1	0	0	2
66	1	1	1	1	0	1	0	2
43	1	1	1	0	1	1	0	2
2	1	1	0	1	1	0	1	2
4	1	1	0	1	0	1	1	2
19	1	1	0	1	1	1	0	2
1	1	1	1	0	0	0	1	3
3	1	0	1	1	1	0	0	3
25	1	1	1	1	0	0	0	3
77	1	1	1	0	1	0	0	3
9	1	1	1	0	0	1	0	3
3	1	1	0	0	0	1	1	3
20	1	1	0	1	1	0	0	3
7	1	1	0	1	0	1	0	3
2	1	1	0	0	1	1	0	3
32	1	1	1	0	0	0	0	4
11	1	0	0	1	1	0	0	4
3	1	1	0	1	0	0	0	4
11	1	1	0	0	1	0	0	4
1	1	1	0	0	0	1	0	4
6	1	0	0	1	0	0	0	5
6	1	0	0	0	1	0	0	5
15	1	1	0	0	0	0	0	5
170	1	0	0	0	0	0	0	6
TOTAL	0	198	319	460	495	689	1241	

1.2 GENERAL QUALITY INDICATORS

Table 15: Descriptive statistics for QCI 1111 [OS], for size-grouped centers.

Center	Total N (missing)	N (%) eligible	Min	P25	P50	P75	Max	Person years	N (%) events	Event rate
TOTAL	3318 (211)	3103 (94%)	0.00	1.47	2.54	3.66	6.57	7915.49	697 (22%)	0.08806
[0-10[	68 (3)	65 (96%)	0.04	1.98	3.21	4.49	6.57	205.34	16 (25%)	0.07792
[10-20[	218 (33)	185 (85%)	0.08	1.39	2.67	3.87	5.23	489.59	47 (25%)	0.09600
[20-40[	422 (17)	405 (96%)	0.01	1.55	2.66	3.61	4.95	1025.73	104 (26%)	0.10139
[40-60[	663 (30)	633 (95%)	0.03	1.44	2.45	3.69	5.61	1605.86	159 (25%)	0.09901
[60-80[	399 (47)	351 (88%)	0.00	1.38	2.52	3.65	5.25	883.78	90 (26%)	0.10184
[80-100[	523 (42)	480 (92%)	0.01	1.11	2.31	3.42	4.95	1107.01	109 (23%)	0.09846
[100-]	1025 (39)	984 (96%)	0.05	1.61	2.61	3.65	5.15	2598.18	172 (17%)	0.06620

Figure 5: (y)pStage-stratified Kaplan-Meier curves for QCI 1111 [OS], estimating the probability of surviving t years after incidence of rectum cancer.

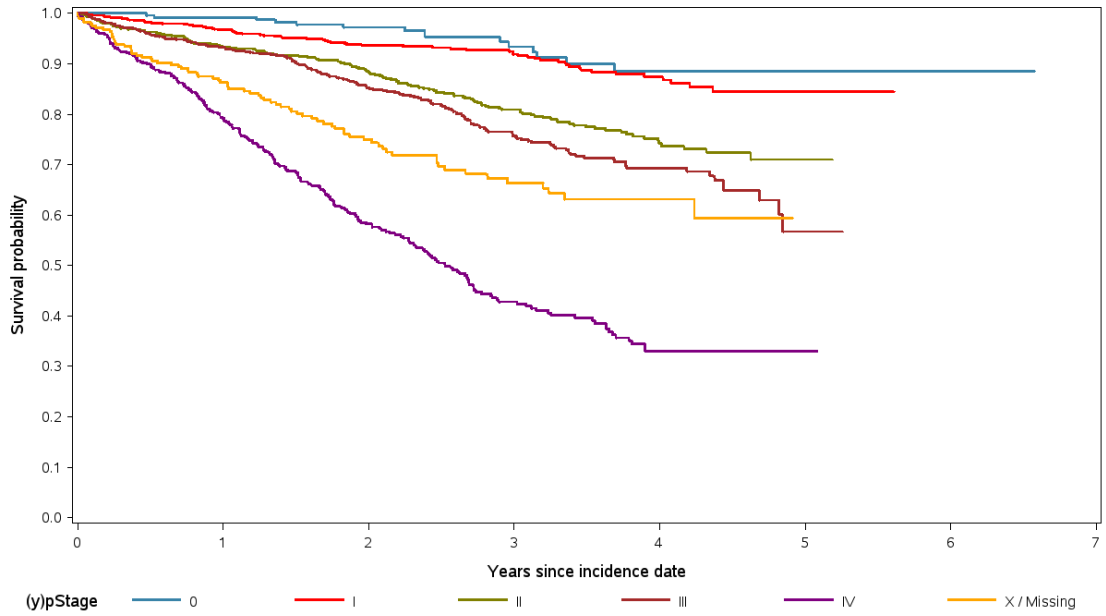


Table 16: Descriptive statistics for QCI 1112 [DSS], for size-grouped centers.
Event 1 represents the event of interest (death with local recurrence or distant metastases) and event 2 represents the competing event (death without local recurrence or distant metastases).

Center	Total N (missing)	N (%) eligible	Min	P25	P50	P75	Max	Person years	N (%) events 1	Event rate 1	N (%) events 2	Event rate 2
TOTAL	3318 (507)	2807 (85%)	0.04	1.65	2.68	3.73	6.57	7528.93	193 (7%)	0.025634	210 (7%)	0.027892
[1-10[	68 (13)	55 (81%)	0.04	2.14	3.77	4.51	6.57	185.57	1 (2%)	0.005389	5 (9%)	0.026943
[10-20[	218 (57)	161 (74%)	0.23	1.54	2.92	4.08	5.23	453.68	9 (6%)	0.019838	14 (9%)	0.030859
[20-40[	422 (58)	364 (86%)	0.04	1.78	2.70	3.71	4.95	974.40	29 (8%)	0.029762	34 (9%)	0.034893
[40-60[	663 (100)	563 (85%)	0.07	1.64	2.63	3.78	5.61	1505.94	44 (8%)	0.029218	46 (8%)	0.030546
[60-80[	399 (84)	314 (79%)	0.07	1.69	2.76	3.76	5.25	846.99	26 (8%)	0.030697	28 (9%)	0.033058
[80-100[	523 (86)	436 (83%)	0.05	1.39	2.45	3.51	4.95	1074.30	28 (6%)	0.026063	37 (8%)	0.034441
[100-]	1025 (109)	914 (89%)	0.05	1.69	2.69	3.71	5.15	2488.05	56 (6%)	0.022508	46 (5%)	0.018488

Figure 6: (y)pStage-stratified cumulative incidence-based survival curves for QCI 1112 [DSS], estimating the probability of surviving rectal cancer or dying without local recurrence nor distant metastasis t years after incidence of rectum cancer.

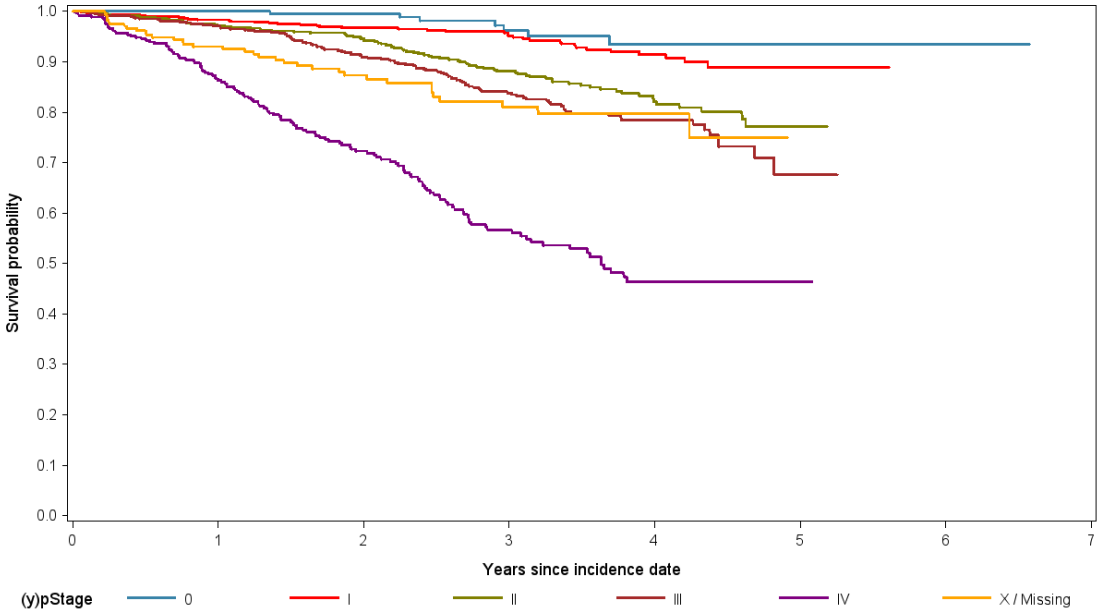


Table 17: Descriptive statistics for QCI 1113 [LRFS], for size-grouped centers.
Event 1 represents the event of interest (local recurrence) and event 2 represents the competing event (death without local recurrence).

Center	Total N (missing)	N (%) eligible	Min	P25	P50	P75	Max	Person years	N (%) events 1	Event rate 1	N (%) events 2	Event rate 2
TOTAL	3318 (1776)	1186 (36%)	0.12	2.25	3.17	4.02	5.61	3654.31	29 (2%)	0.007936	98 (8%)	0.026818
[1-10[	68 (52)	12 (18%)	1.62	3.10	3.67	4.26	5.29	43.37	0 (0%)	0.000000	1 (8%)	0.023059
[10-20[	218 (143)	61 (28%)	0.44	1.93	3.38	4.36	5.23	195.11	3 (5%)	0.015376	7 (11%)	0.035878
[20-40[	422 (186)	169 (40%)	0.37	1.94	2.70	3.59	4.94	465.62	8 (5%)	0.017181	13 (8%)	0.027920
[40-60[	663 (367)	234 (35%)	0.12	2.21	3.30	4.17	5.61	717.77	3 (1%)	0.004180	24 (10%)	0.033437
[60-80[	399 (229)	124 (31%)	0.67	2.46	3.36	3.99	5.25	393.34	1 (1%)	0.002542	13 (10%)	0.033050
[80-100[	523 (292)	179 (34%)	0.56	2.37	3.21	3.95	4.88	557.40	5 (3%)	0.008970	11 (6%)	0.019735
[100-]	1025 (507)	407 (40%)	0.51	2.27	3.17	4.16	5.15	1281.70	9 (2%)	0.007022	29 (7%)	0.022626

Figure 7: (y)pStage-stratified cumulative incidence-based survival curves for QCI 1113 [LRFS], estimating the probability of surviving rectal cancer or not having a local recurrence t years after incidence of rectum cancer.

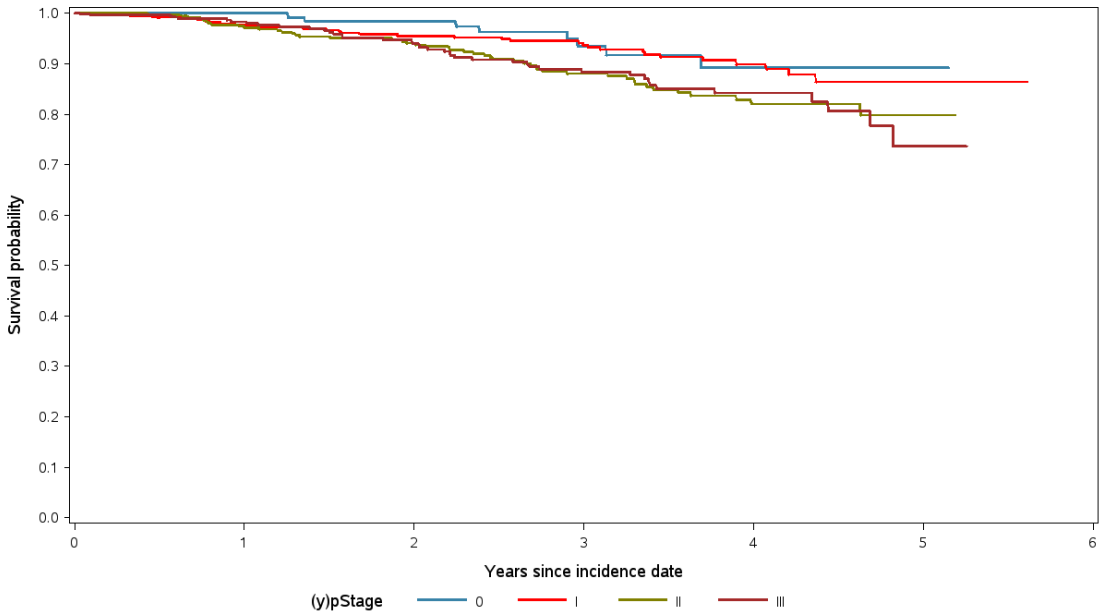
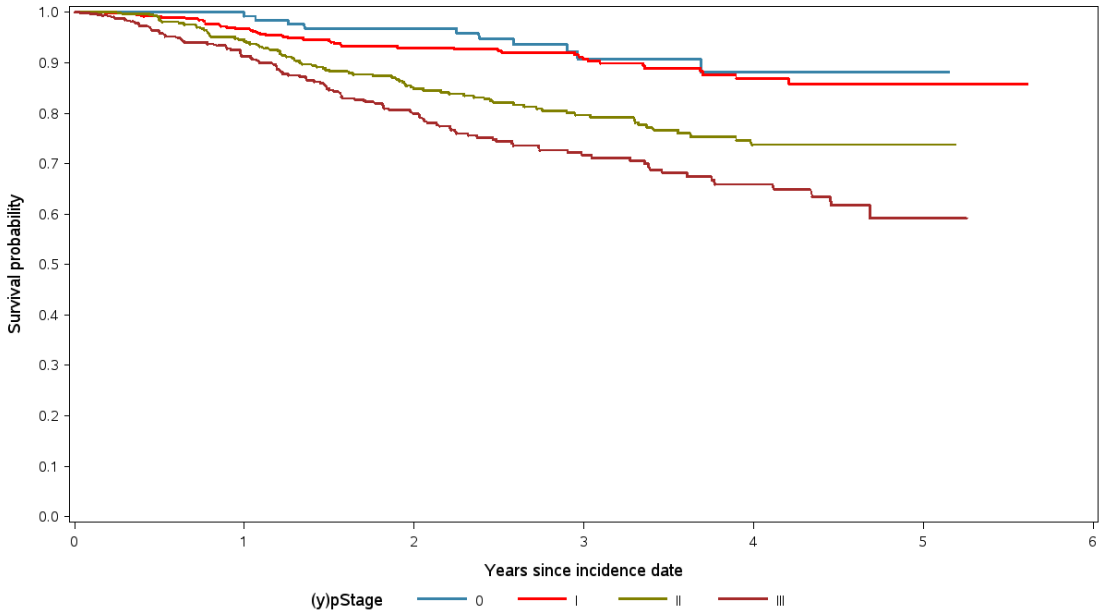


Table 18: Descriptive statistics for QCI 1113b [DFS], for size-grouped centers.

Center	Total N (missing)	N (%) eligible	Min	P25	P50	P75	Max	Person years	N (%) events	Event rate
TOTAL	3318 (1680)	1234 (37%)	0.12	1.98	2.95	3.90	5.61	3581.93	226 (18%)	0.063094
[1-10[	68 (51)	13 (19%)	1.23	3.07	3.66	4.02	5.29	44.59	2 (15%)	0.044849
[10-20[	218 (141)	63 (29%)	0.44	1.33	3.15	4.32	5.23	184.00	16 (25%)	0.086959
[20-40[	422 (173)	175 (41%)	0.30	1.77	2.58	3.53	4.94	458.13	34 (19%)	0.074215
[40-60[	663 (340)	245 (37%)	0.12	1.87	3.13	3.94	5.61	719.77	44 (18%)	0.061131
[60-80[	399 (217)	131 (33%)	0.38	1.98	3.27	3.95	5.25	387.63	30 (23%)	0.077393
[80-100[	523 (278)	185 (35%)	0.24	2.29	3.02	3.86	4.88	550.00	28 (15%)	0.050909
[100-]	1025 (480)	422 (41%)	0.18	2.02	2.95	3.90	5.15	1237.82	72 (17%)	0.058167

Figure 8: (y)pStage-stratified Kaplan-Meier curves for QCI 1113b [DFS], estimating the probability of surviving or not relapsing from rectal cancer t years after incidence of rectum cancer.



1.3 QUALITY INDICATORS RELATED TO DIAGNOSIS AND STAGING

Table 19: QCI 1211 [%DocDist] (process): Proportion of patients with a documented distance from the anal verge. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (0)	3318 (100%)	2999 (90%)
[1-10[	68 (0)	68 (100%)	65 (96%)
[10-20[	218 (0)	218 (100%)	172 (79%)
[20-40[	422 (0)	422 (100%)	391 (93%)
[40-60[	663 (0)	663 (100%)	612 (92%)
[60-80[	399 (0)	399 (100%)	334 (84%)
[80-100[	523 (0)	523 (100%)	470 (90%)
[100-]	1025 (0)	1025 (100%)	955 (93%)

Figure 9: QCI 1211 [%DocDist] (process): Proportion of patients with a documented distance from the anal verge.
Above: Unadj. excess probability (%), relative to the average center.

Below: Prevalence (%) among eligible cases.

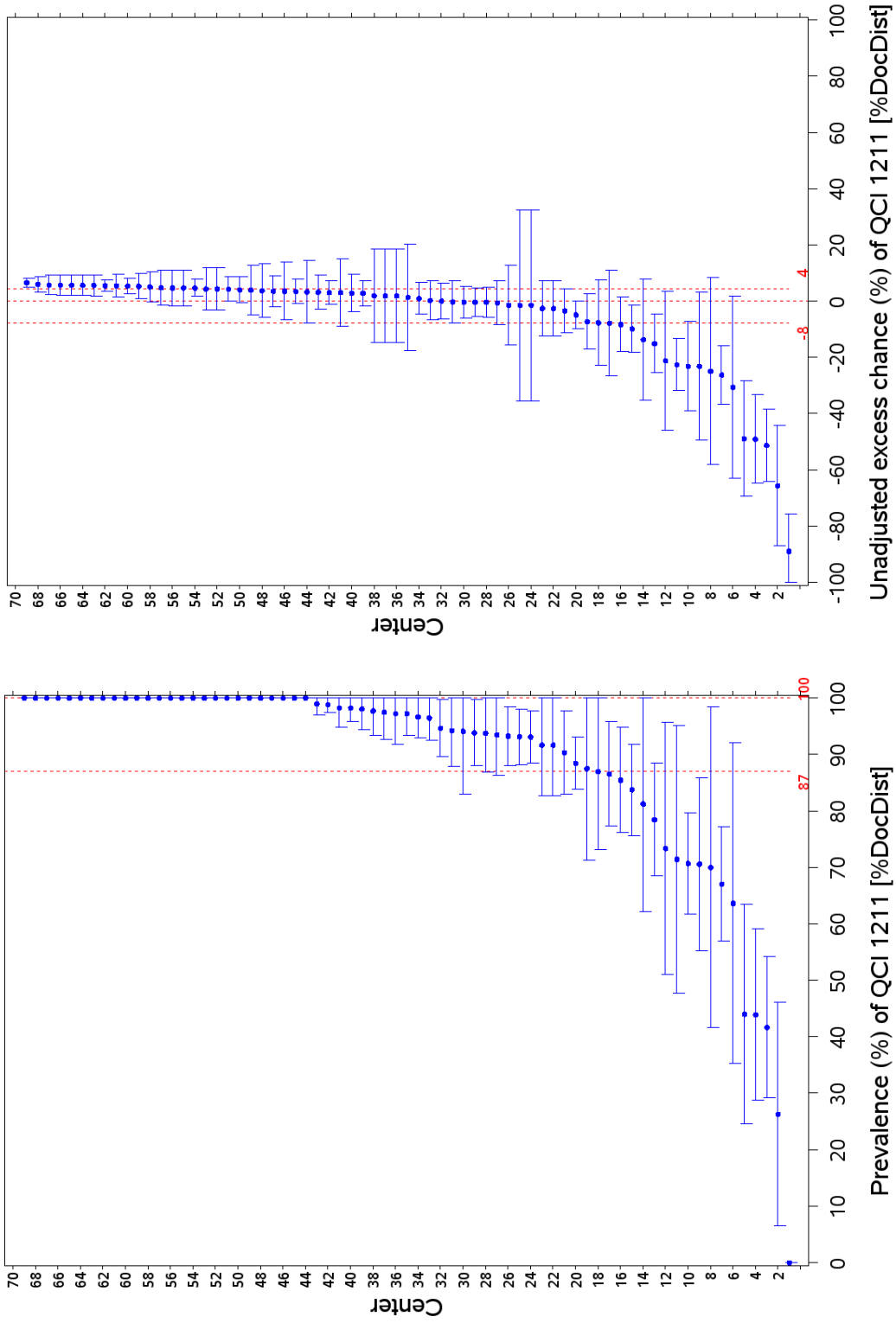


Table 20: QCI 1212 [%CT_Preop] (process): Proportion of patients in whom a CT of the abdomen and RX or CT thorax was performed before any treatment.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (457)	322 (10%)	254 (79%)
[1-10[	68 (8)	2 (3%)	2 (100%)
[10-20[	218 (45)	31 (14%)	27 (87%)
[20-40[	422 (47)	23 (5%)	22 (96%)
[40-60[	663 (82)	53 (8%)	26 (49%)
[60-80[	399 (60)	70 (18%)	62 (89%)
[80-100[	523 (101)	63 (12%)	42 (67%)
[100-]	1025 (114)	80 (8%)	73 (91%)

Figure 10: QCI 1212 [%CT_Preop] (process): Proportion of patients in whom a CT of the abdomen and RX or CT thorax was performed before any treatment.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

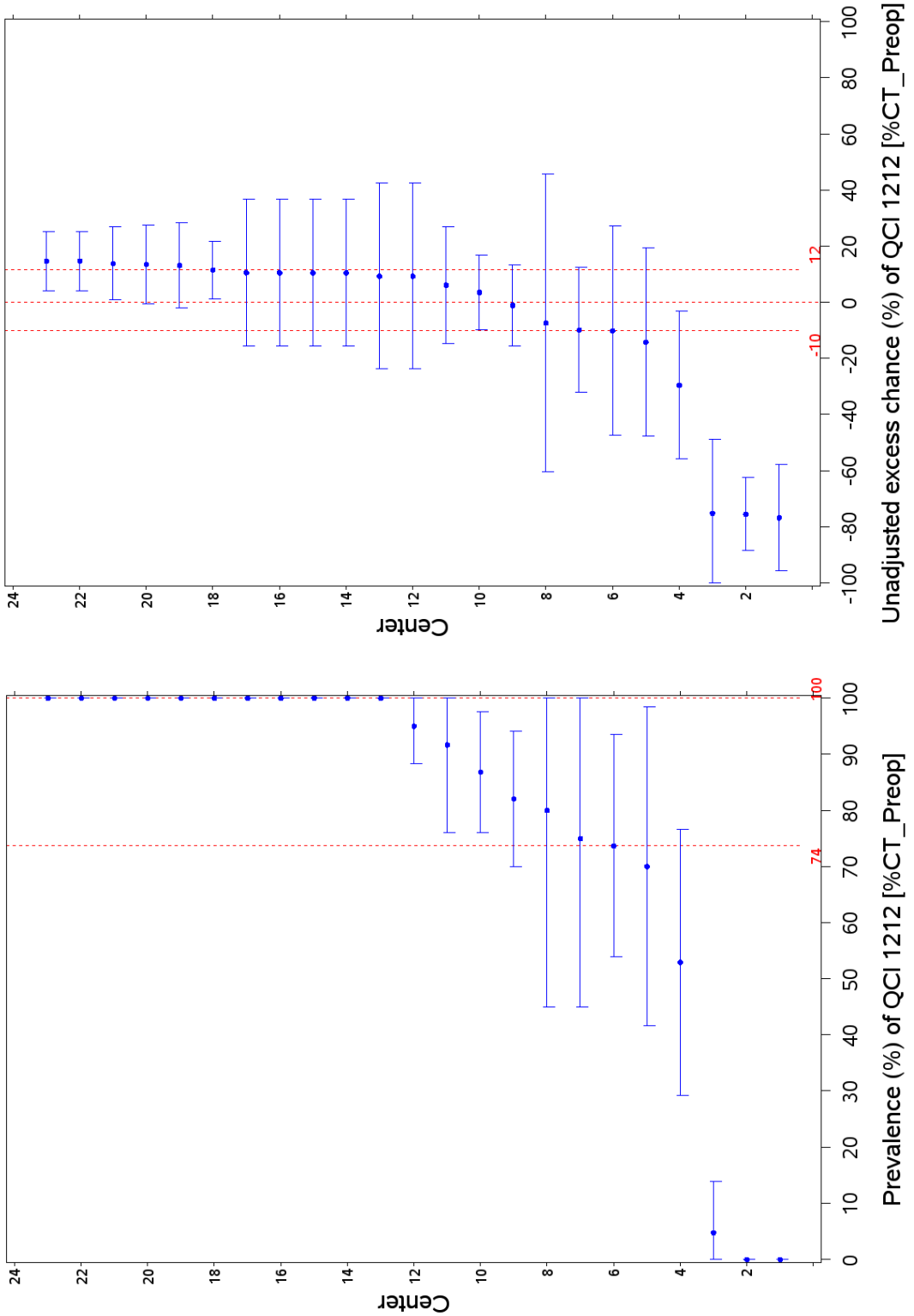


Table 21: QCI 1213 [%CEA_Preop] (process): Proportion of patients in whom a CEA was performed before any treatment.

Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (0)	3318 (100%)	2699 (81%)
[1-10[	68 (0)	68 (100%)	61 (90%)
[10-20[	218 (0)	218 (100%)	164 (75%)
[20-40[	422 (0)	422 (100%)	355 (84%)
[40-60[	663 (0)	663 (100%)	529 (80%)
[60-80[	399 (0)	399 (100%)	270 (68%)
[80-100[	523 (0)	523 (100%)	408 (78%)
[100-]	1025 (0)	1025 (100%)	912 (89%)

Figure 11: QCI 1213 [%CEA_Preop] (process): Proportion of patients in whom a CEA was performed before any treatment.

Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

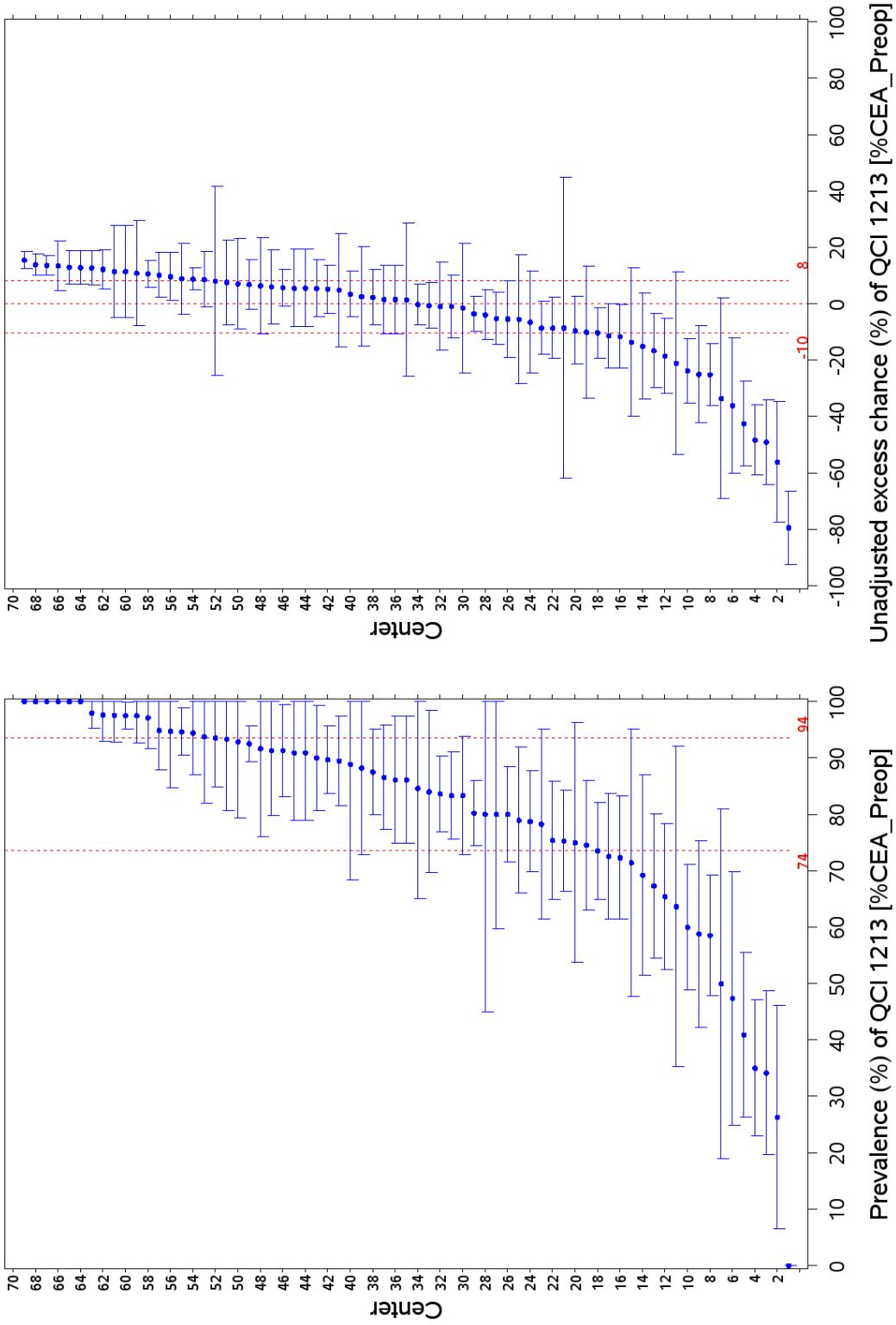


Table 22: QCI 1214 [%Preop_Bowel_Im] (process): Proportion of patients undergoing elective surgery that had preoperative complete large bowel-imaging.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (455)	2811 (85%)	2764 (98%)
[1-10[	68 (8)	58 (85%)	58 (100%)
[10-20[	218 (45)	171 (78%)	167 (98%)
[20-40[	422 (47)	361 (86%)	359 (99%)
[40-60[	663 (81)	571 (86%)	561 (98%)
[60-80[	399 (60)	333 (83%)	321 (96%)
[80-100[	523 (101)	411 (79%)	402 (98%)
[100-]	1025 (113)	906 (88%)	896 (99%)

Figure 12: QCI 1214 [%Preop_Bowel_Im] (process): Proportion of patients undergoing elective surgery that had preoperative complete large bowel-imaging.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

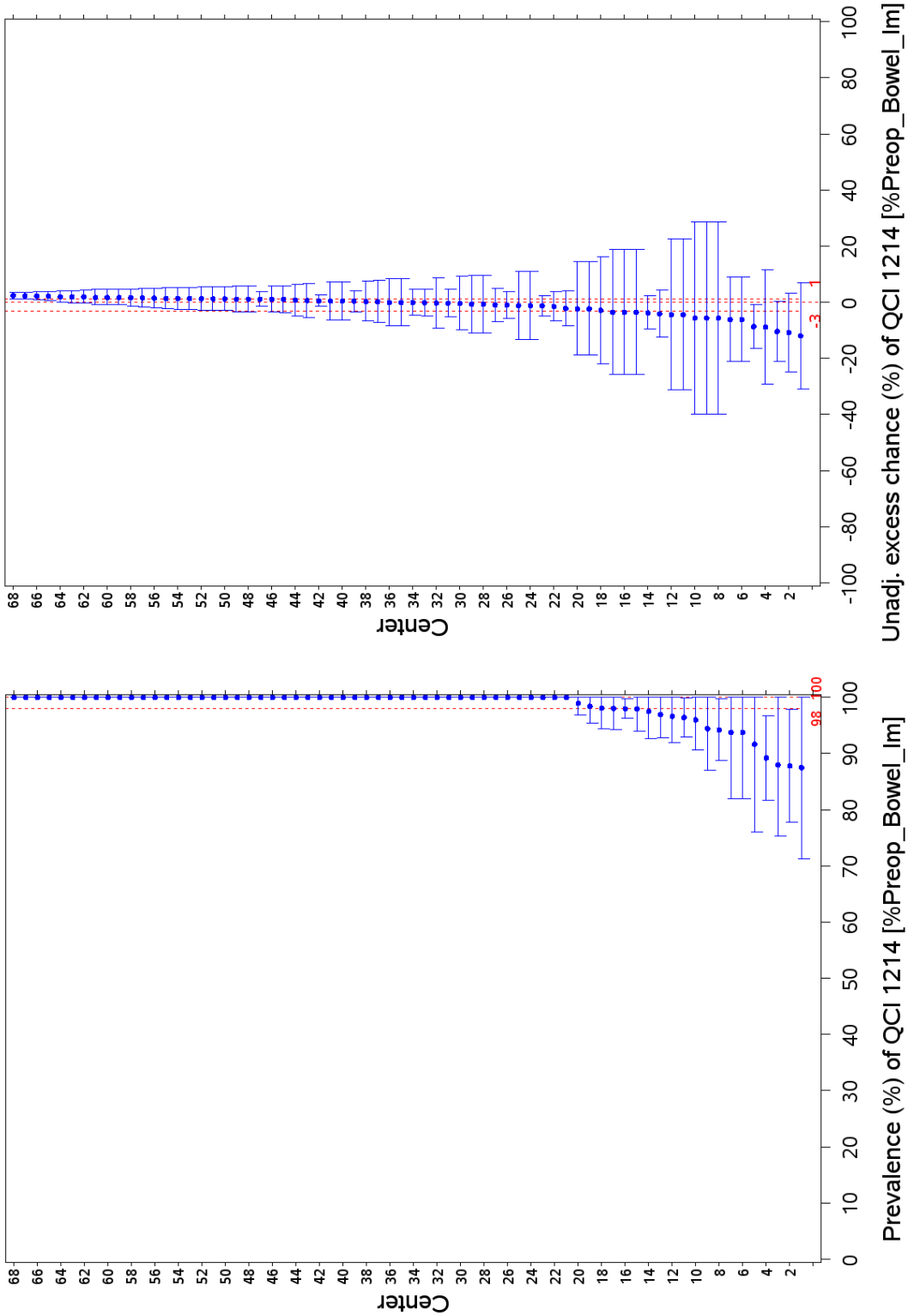


Table 23: QCI 1214b [%TRUS_cT12] (process): Use of TRUS in cT1/cT2.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (649)	74 (2%)	61 (82%)
[1-10[	68 (18)	0 (0%)	
[10-20[	218 (53)	4 (2%)	3 (75%)
[20-40[	422 (86)	9 (2%)	9 (100%)
[40-60[	663 (142)	15 (2%)	11 (73%)
[60-80[	399 (82)	14 (4%)	12 (86%)
[80-100[	523 (127)	11 (2%)	7 (64%)
[100-]	1025 (141)	21 (2%)	19 (90%)

Figure 13: QCI 1214b [%TRUS_cT12] (process): Use of TRUS in cT1/cT2.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

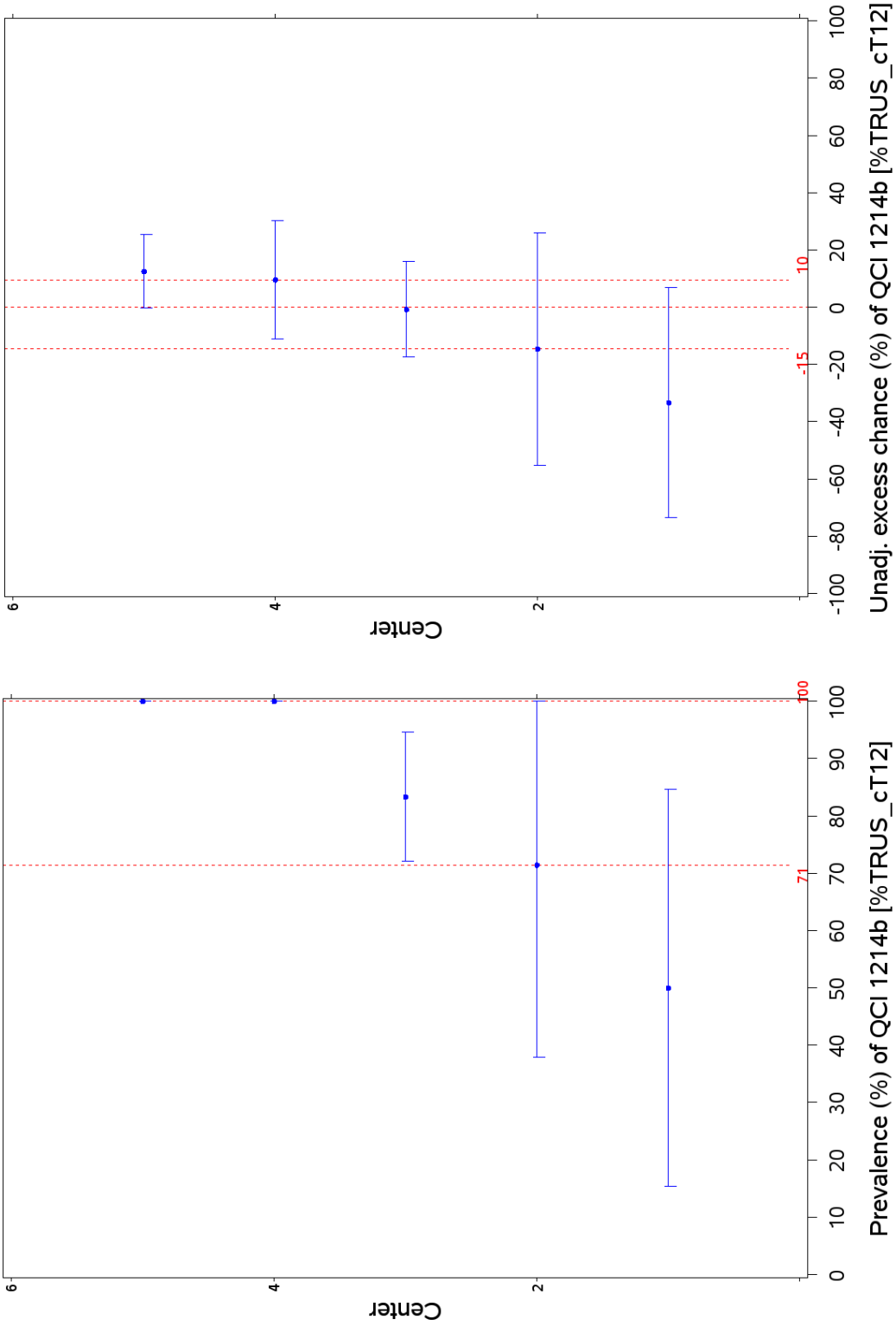


Table 24: QCI 1214c [%MR_cII/III] (process): Use of MRI in cStage II or III.

Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (2135)	103 (3%)	94 (91%)
[1-10[	68 (43)	1 (1%)	1 (100%)
[10-20[	218 (170)	2 (1%)	1 (50%)
[20-40[	422 (278)	8 (2%)	8 (100%)
[40-60[	663 (469)	12 (2%)	9 (75%)
[60-80[	399 (271)	23 (6%)	19 (83%)
[80-100[	523 (356)	26 (5%)	26 (100%)
[100-]	1025 (548)	31 (3%)	30 (97%)

Figure 14: QCI 1214c [%MR_cII/III] (process): Use of MRI in cStage II or III.

Above: Unadj. excess probability (%), relative to the average center. Below: Prevalence (%) among eligible cases.

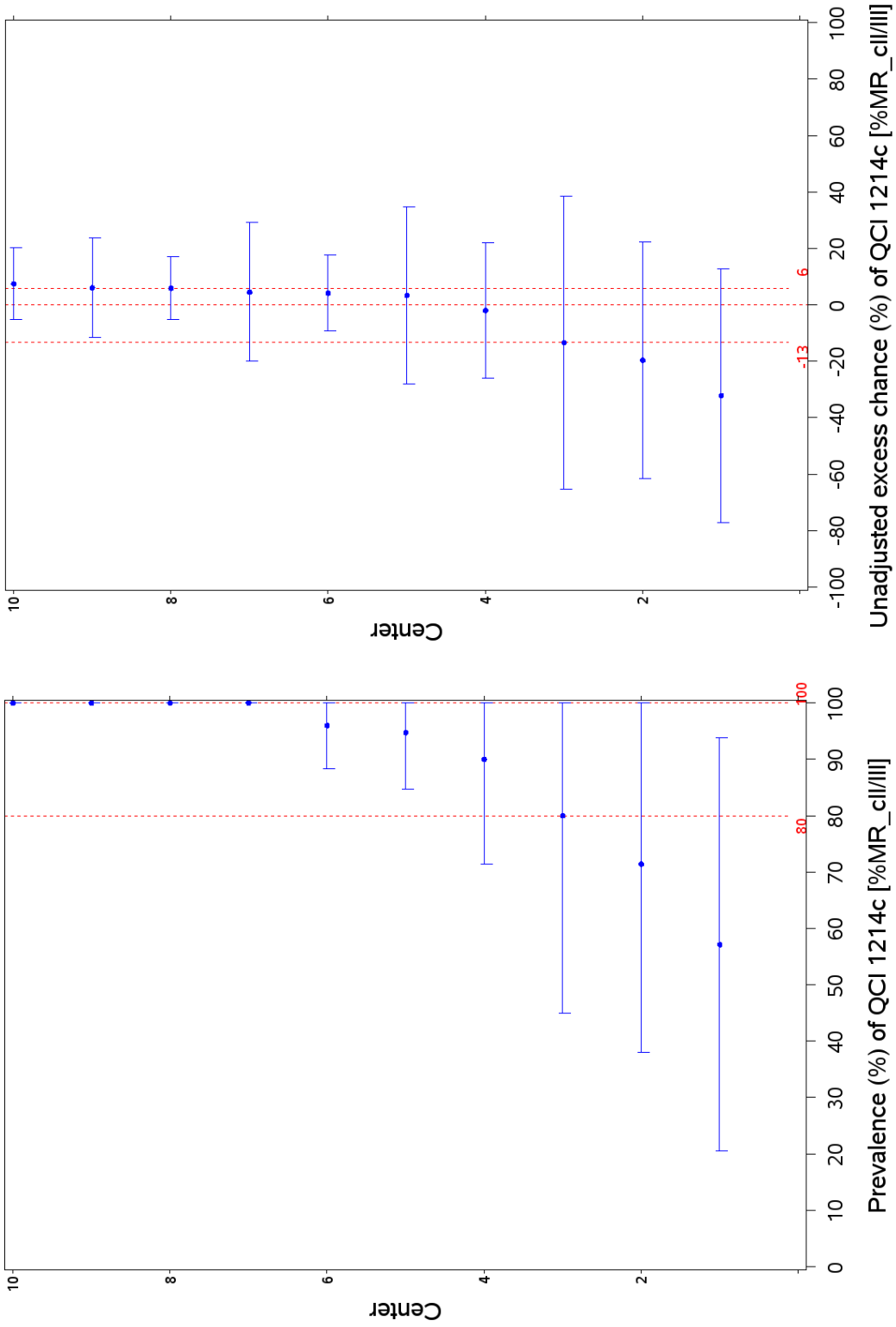


Table 25: QCI 1215 [%Preop_Im] (process): Proportion of patients in whom a TRUS and pelvic CT and/or pelvic MRI was performed before any treatment.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (0)	435 (13%)	264 (61%)
[1-10[	68 (0)	6 (9%)	4 (67%)
[10-20[	218 (0)	42 (19%)	14 (33%)
[20-40[	422 (0)	31 (7%)	20 (65%)
[40-60[	663 (0)	79 (12%)	37 (47%)
[60-80[	399 (0)	94 (24%)	64 (68%)
[80-100[	523 (0)	89 (17%)	52 (58%)
[100-]	1025 (0)	94 (9%)	73 (78%)

Figure 15: QCI 1215 [%Preop_Im] (process): Proportion of patients in whom a TRUS and pelvic CT and/or pelvic MRI was performed before any treatment.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

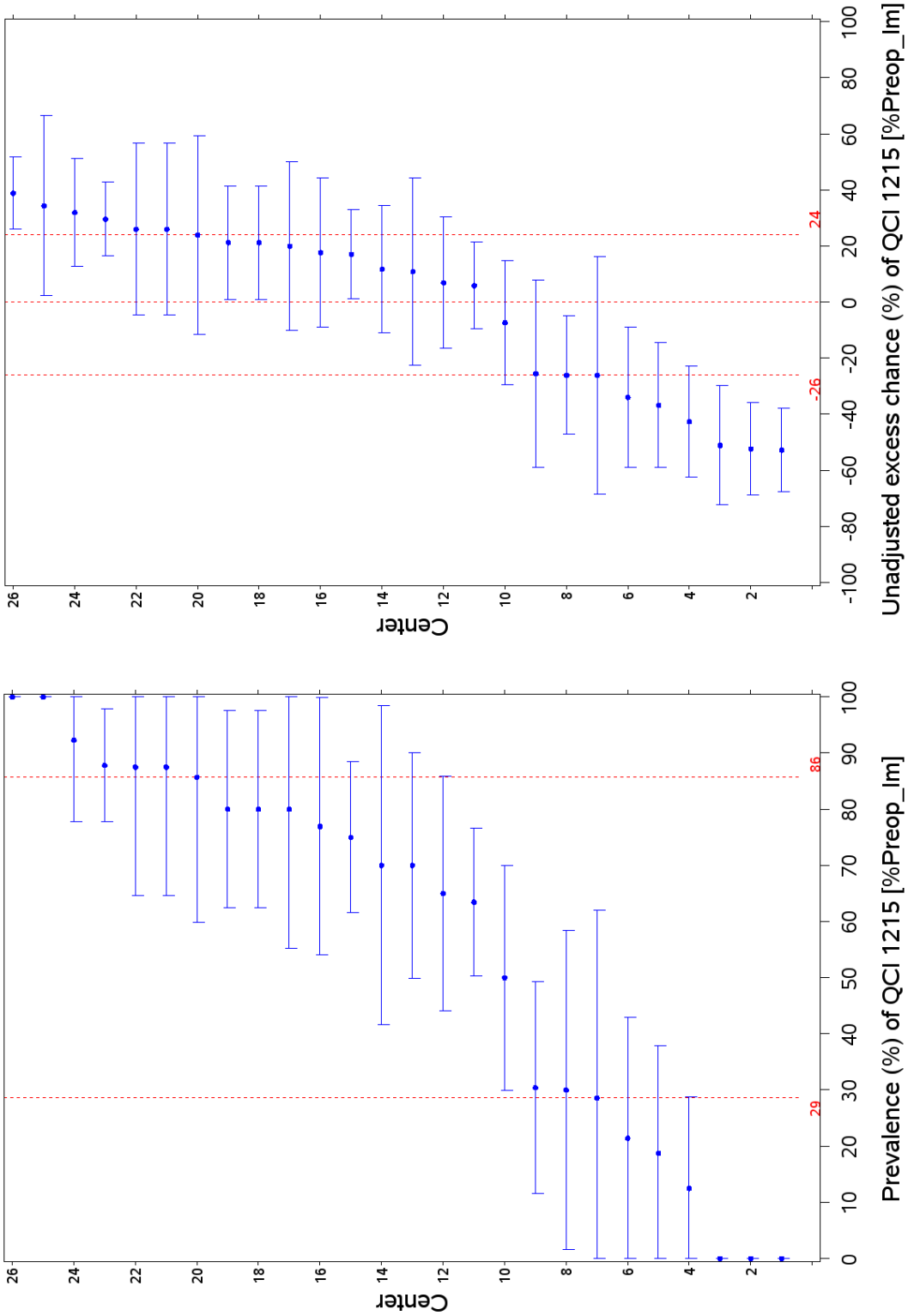


Table 26: QCI 1216 [%cCRM_rep] (process): Proportion of patients with cStage II-III RC that have a reported cCRM.

Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (650)	1950 (59%)	501 (26%)
[1-10[	68 (19)	38 (56%)	4 (11%)
[10-20[	218 (52)	120 (55%)	20 (17%)
[20-40[	422 (89)	229 (54%)	37 (16%)
[40-60[	663 (154)	364 (55%)	62 (17%)
[60-80[	399 (92)	238 (60%)	34 (14%)
[80-100[	523 (132)	284 (54%)	119 (42%)
[100-]	1025 (112)	677 (66%)	225 (33%)

Figure 16: QCI 1216 [%cCRM_rep] (process): Proportion of patients with cStage II-III RC that have a reported cCRM.

Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

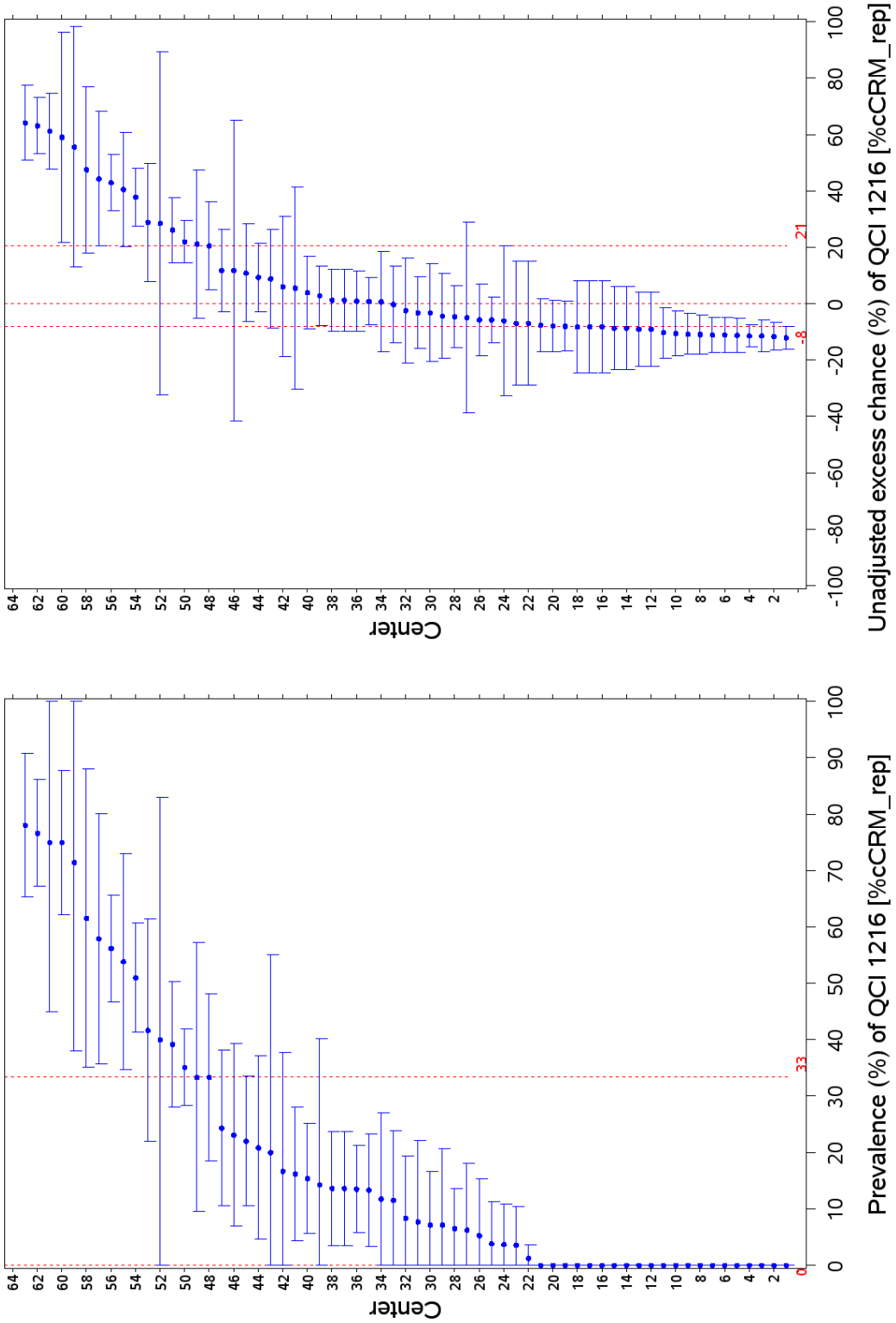


Table 27: QCI 1216b [cM0_Acc] (process): Accuracy of cM0 staging. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (2451)	634 (19%)	35 (6%)
[1-10[	68 (63)	4 (6%)	0 (0%)
[10-20[	218 (177)	31 (14%)	1 (3%)
[20-40[	422 (277)	108 (26%)	5 (5%)
[40-60[	663 (522)	92 (14%)	10 (11%)
[60-80[	399 (318)	50 (13%)	3 (6%)
[80-100[	523 (404)	86 (16%)	2 (2%)
[100-]	1025 (690)	263 (26%)	14 (5%)

Figure 17: QCI 1216b [cM0_Acc] (process): Accuracy of cM0 staging.

Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

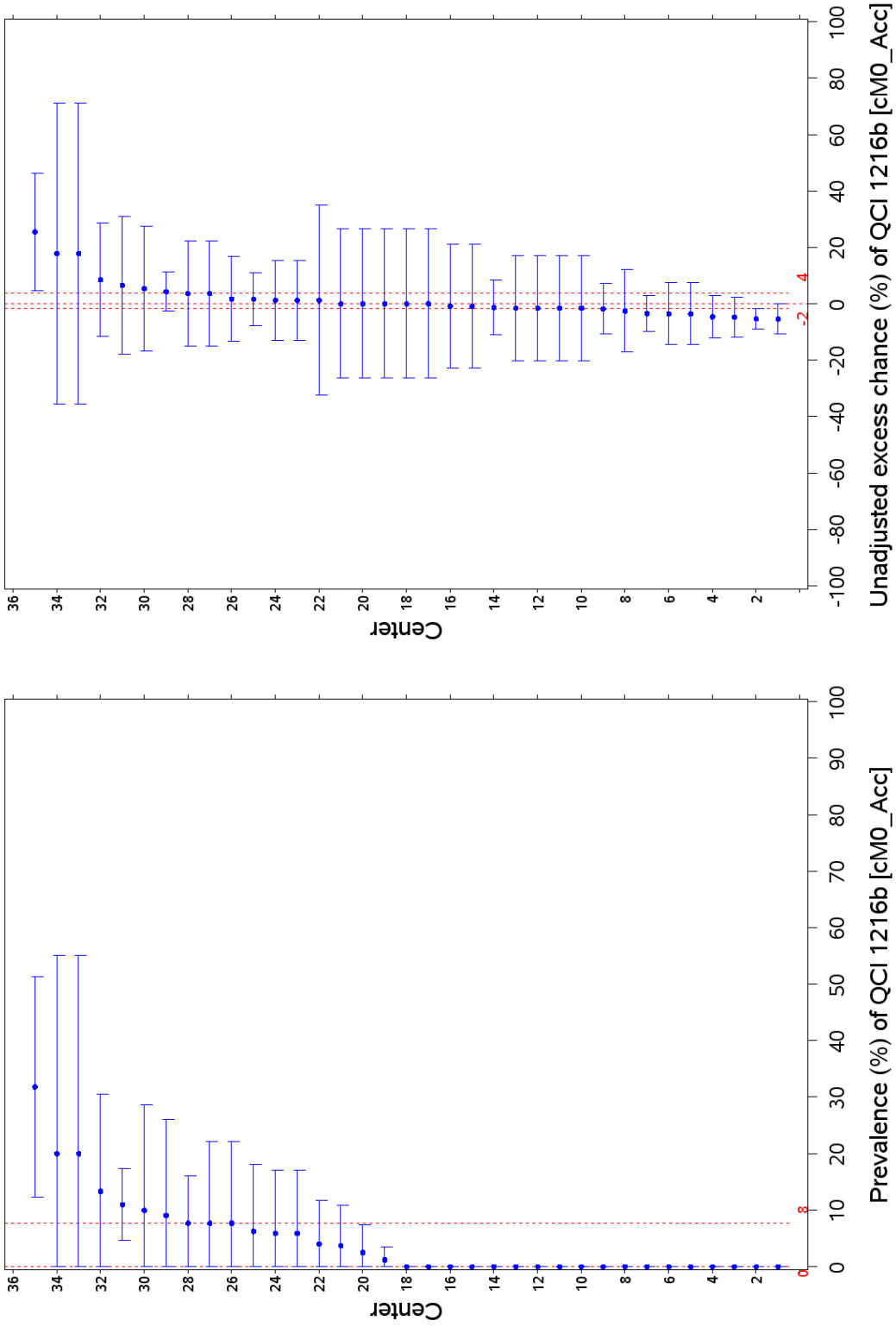


Table 28: QCI 1217 [Time_histo_1ther] (process): Time between first histopathologic diagnosis and first treatment (in days).

Statistical summary of the distribution of this QCI.

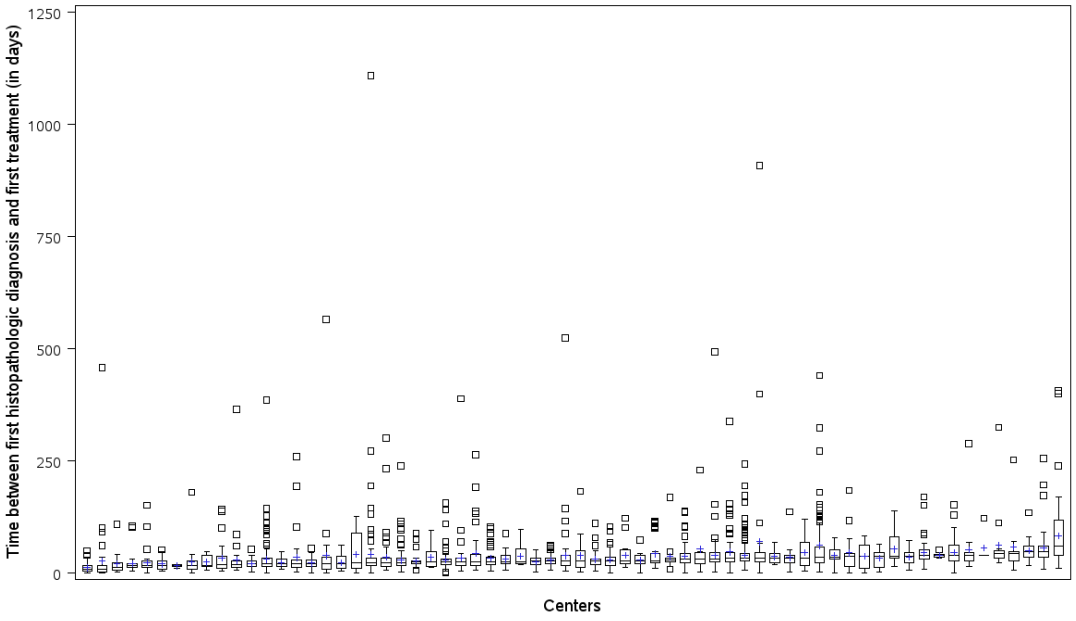
Center	Total N (missing)	N (%) eligible	Min	P25	P50	P75	Max
TOTAL	3318 (631)	2687 (81%)	0	17	27	40	1109
[1-10[	68 (12)	56 (82%)	1	19	33	47	230
[10-20[	218 (48)	170 (78%)	0	19	34	46	325
[20-40[	422 (90)	332 (79%)	0	18	26	40	909
[40-60[	663 (114)	549 (83%)	0	14	22	32	566
[60-80[	399 (80)	319 (80%)	0	20	30	42	524
[80-100[	523 (129)	394 (75%)	0	12	22	33	441
[100-]	1025 (158)	867 (85%)	0	20	29	43	1109

Table 29: Truncated QCI 1217 [Time_histo_1ther] (process): Time between first histopathologic diagnosis and first treatment (in days), truncated at 180 days.

Statistical summary of the distribution of this truncated QCI.

Center	Total N (missing)	N (%) eligible	Min	P25	P50	P75	Max
TOTAL	3318 (631)	2687 (81%)	0	17	27	40	180
[1-10[	68 (12)	56 (82%)	1	19	33	47	180
[10-20[	218 (48)	170 (78%)	0	19	34	46	180
[20-40[	422 (90)	332 (79%)	0	18	26	40	180
[40-60[	663 (114)	549 (83%)	0	14	22	32	180
[60-80[	399 (80)	319 (80%)	0	20	30	42	180
[80-100[	523 (129)	394 (75%)	0	12	22	33	180
[100-]	1025 (158)	867 (85%)	0	20	29	43	180

Figure 18: Box plots of QCI 1217 [Time_histo_1ther] (process) in individual centers, sorted by median number of days between biopsy and first treatment ('-' = median; '+' = mean; '□' = outlying observation).
Above: Original values.
Below: Values truncated at 180 days.



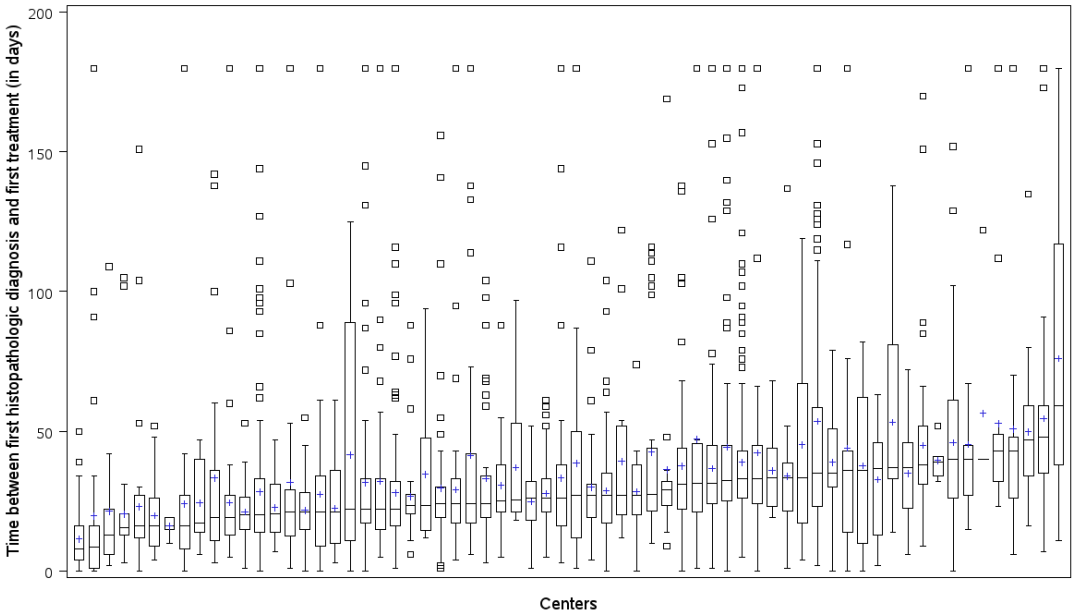
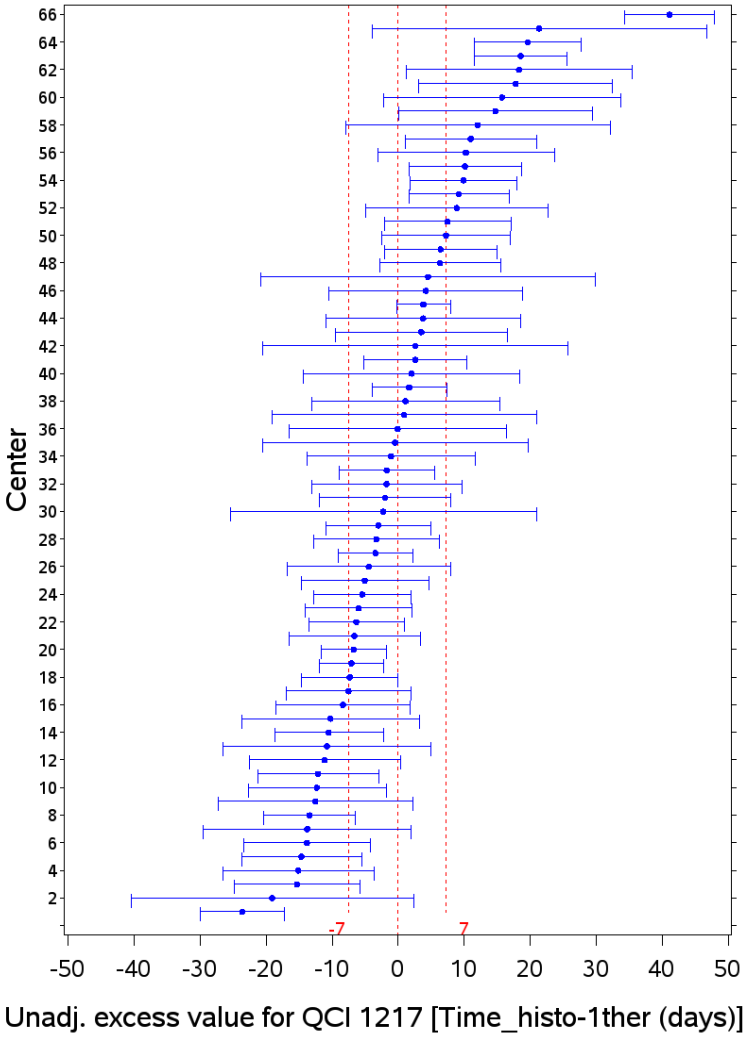


Figure 19: QCI 1217 [Time_histo_1ther] (process): Time between first histopathologic diagnosis and first treatment (in days). Unadjusted excess (truncated) number of days, relative to the average center.



1.4 QUALITY INDICATORS RELATED TO NEOADJUVANT TREATMENT

Table 30: QCI 1221 [%Preop_RT] (process): Proportion of cStage II-III patients that received a neoadjuvant pelvic RT.

Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (556)	1830 (55%)	1360 (74%)
[1-10[	68 (18)	34 (50%)	29 (85%)
[10-20[	218 (48)	116 (53%)	80 (69%)
[20-40[	422 (74)	208 (49%)	155 (75%)
[40-60[	663 (127)	332 (50%)	222 (67%)
[60-80[	399 (80)	233 (58%)	162 (70%)
[80-100[	523 (116)	271 (52%)	184 (68%)
[100-]	1025 (93)	636 (62%)	528 (83%)

Figure 20: QCI 1221 [%Preop_RT] (process): Proportion of cStage II-III patients that received a neoadjuvant pelvic RT.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

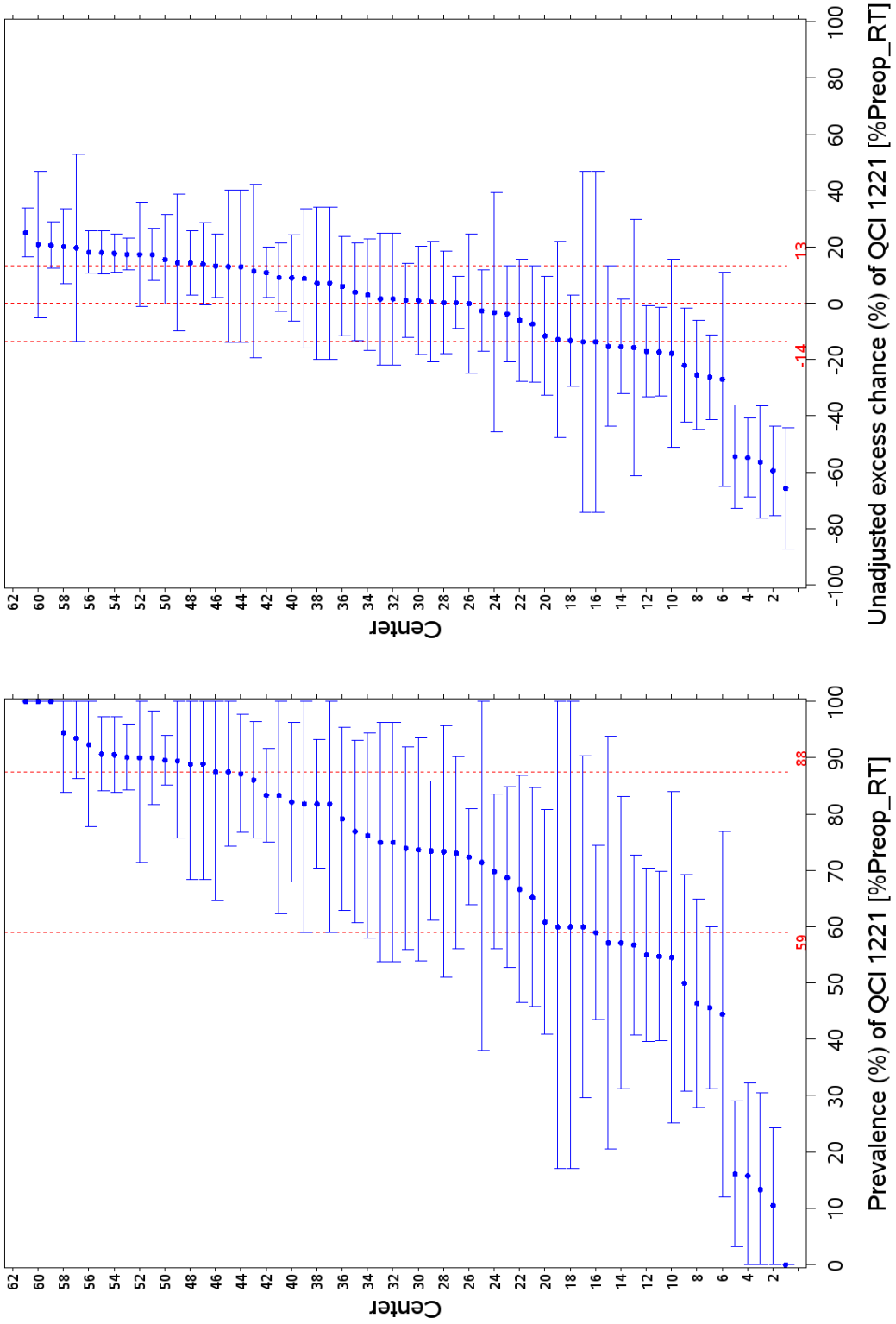
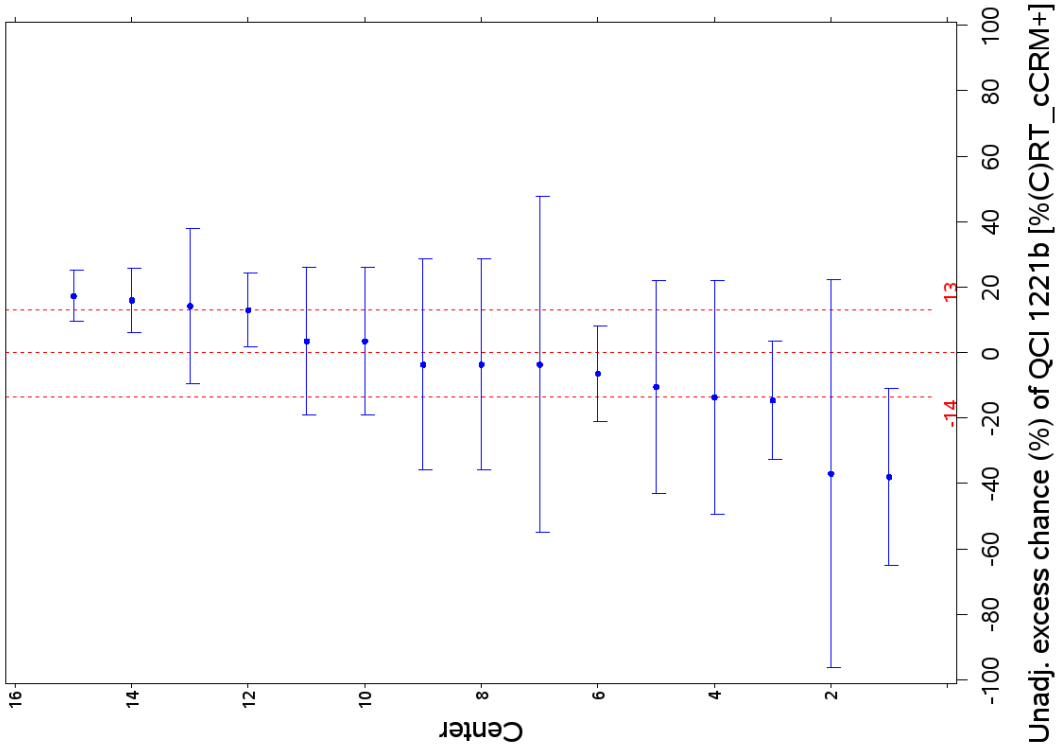


Table 31: QCI 1221b [%(C)RT_cCRM+] (process): Proportion of patients with cCRM ≤ 2 mm on MRI/CT that received long course neoadjuvant radio(chemo)therapy.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (2720)	286 (9%)	231 (81%)
[1-10[	68 (64)	2 (3%)	2 (100%)
[10-20[	218 (191)	14 (6%)	11 (79%)
[20-40[	422 (370)	24 (6%)	18 (75%)
[40-60[	663 (584)	31 (5%)	24 (77%)
[60-80[	399 (362)	17 (4%)	10 (59%)
[80-100[	523 (384)	54 (10%)	45 (83%)
[100-]	1025 (765)	144 (14%)	121 (84%)

Figure 21: QCI 1221b [%(C)RT_cCRM+] (process): Proportion of patients with cCRM ≤ 2 mm on MRI/CT that received long course neoadjuvant radio(chemo)therapy.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.



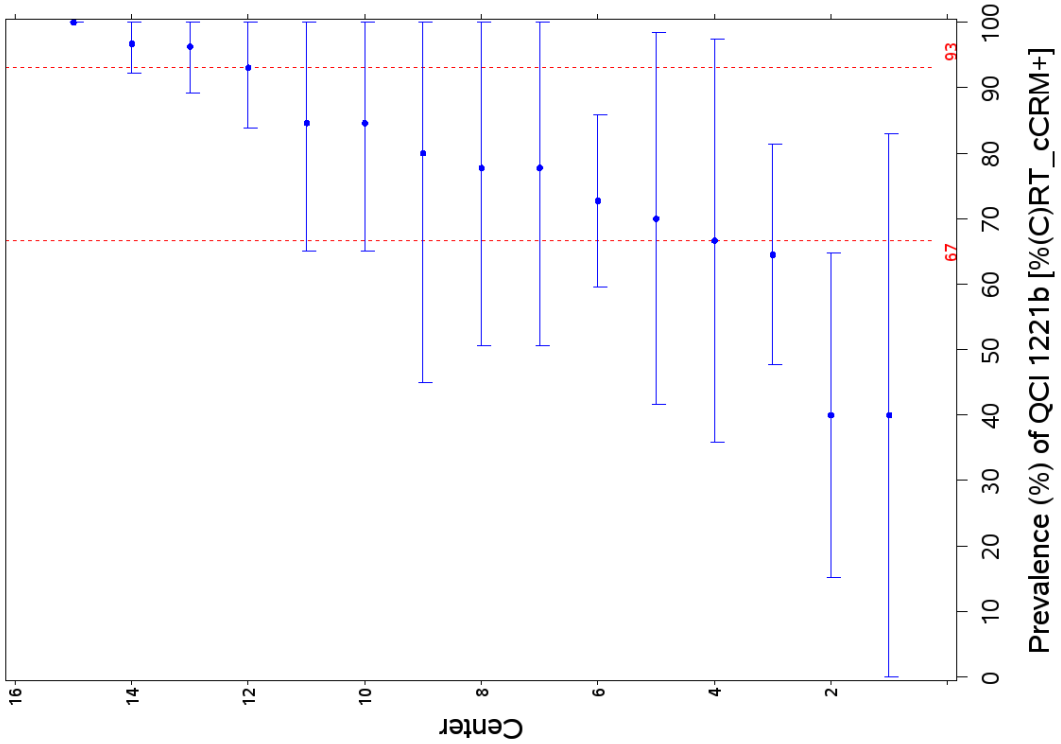


Table 32: QCI 1221c [%Preop_RT_cl] (process): Proportion of patients with cStage I that received neoadjuvant radio(chemo)therapy.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (556)	344 (10%)	60 (17%)
[1-10[	68 (18)	4 (6%)	0 (0%)
[10-20[	218 (48)	19 (9%)	3 (16%)
[20-40[	422 (74)	46 (11%)	10 (22%)
[40-60[	663 (127)	66 (10%)	9 (14%)
[60-80[	399 (80)	30 (8%)	1 (3%)
[80-100[	523 (116)	64 (12%)	9 (14%)
[100-]	1025 (93)	115 (11%)	28 (24%)

Figure 22: QCI 1221c [%Preop_RT_cl] (process): Proportion of patients with cStage I that received neoadjuvant radio(chemo)therapy.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

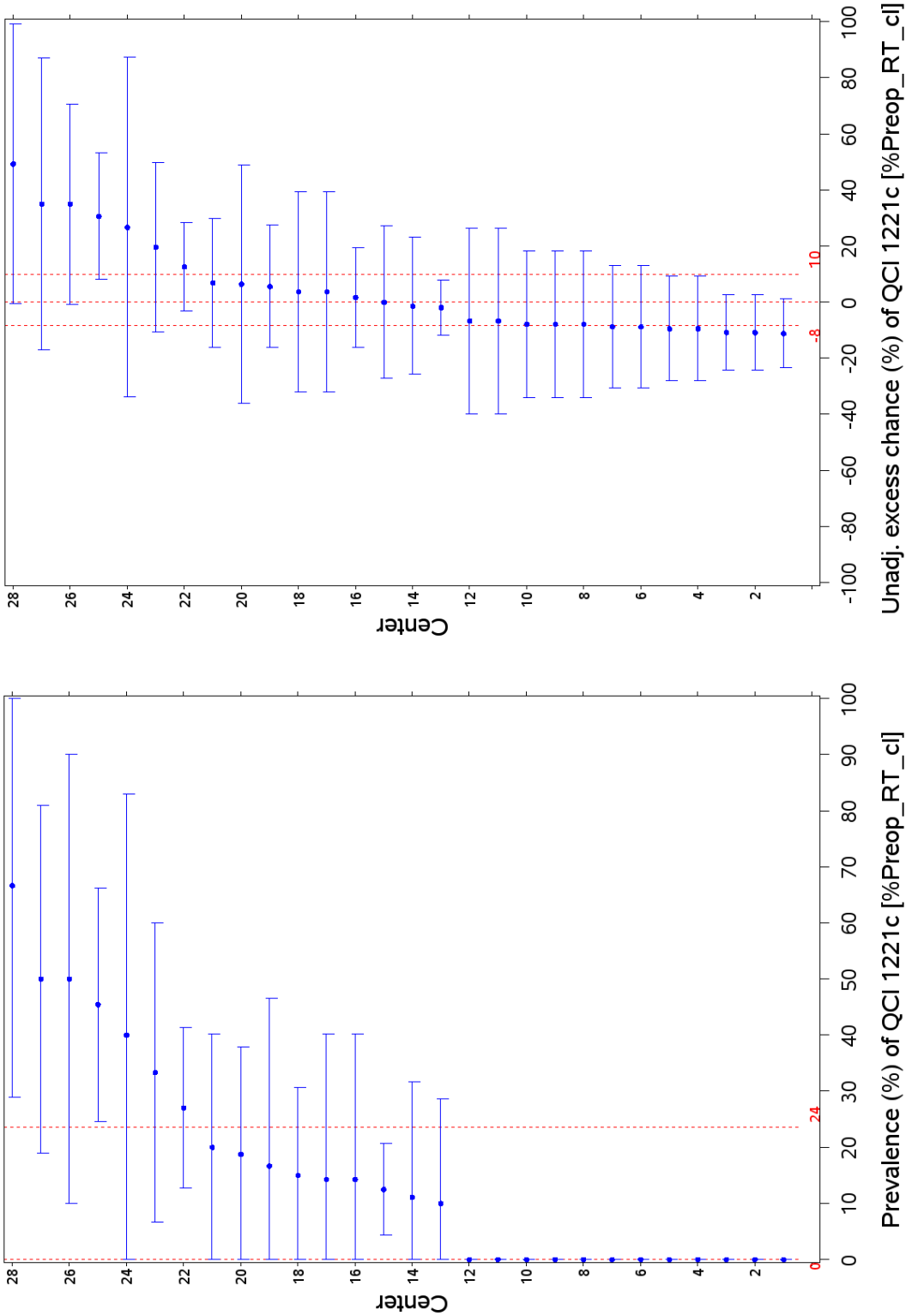


Table 33: QCI 1224 [%Preop_cont_5FU] (process): Proportion of cStage II-III patients treated with neoadjuvant 5-FU based chemoradiation, that received a continuous infusion of 5-FU. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (796)	469 (14%)	425 (91%)
[1-10[	68 (24)	16 (24%)	13 (81%)
[10-20[	218 (57)	26 (12%)	26 (100%)
[20-40[	422 (115)	69 (16%)	68 (99%)
[40-60[	663 (194)	79 (12%)	71 (90%)
[60-80[	399 (100)	54 (14%)	44 (81%)
[80-100[	523 (145)	75 (14%)	72 (96%)
[100-]	1025 (161)	150 (15%)	131 (87%)

Figure 23: QCI 1224 [%Preop_cont_5FU] (process): Proportion of cStage II-III patients treated with neoadjuvant 5-FU based chemoradiation, that received a continuous infusion of 5-FU. Above: Unadj. excess probability (%), relative to the average center. Below: Prevalence (%) among eligible cases.

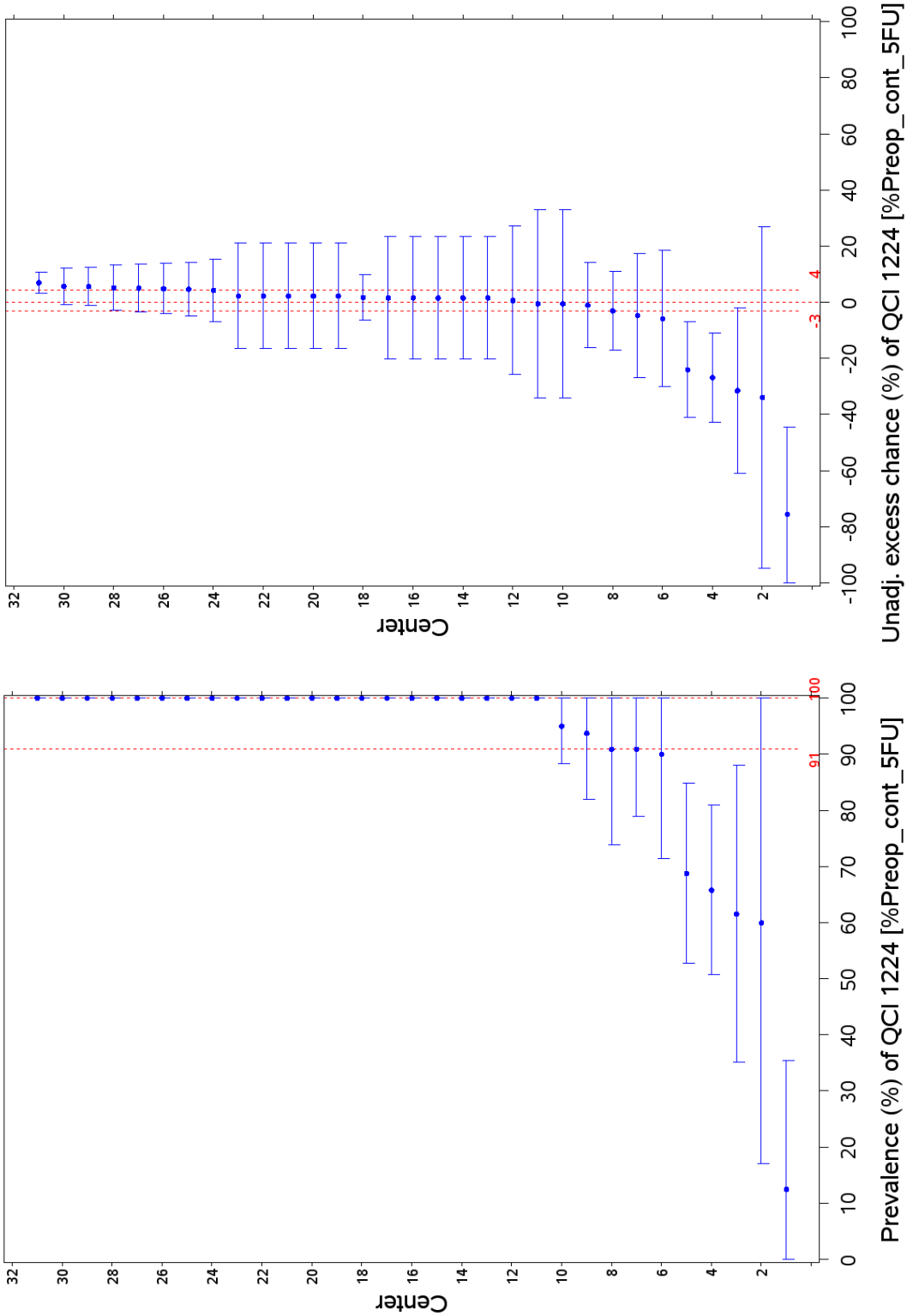


Table 34: QCI 1225 [%Completed_preop_RT] (process): Proportion of cStage II-III patients treated with a long course of preoperative pelvic RT or chemoradiation within the planned timing. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (796)	1196 (36%)	1158 (97%)
[1-10[	68 (24)	28 (41%)	28 (100%)
[10-20[	218 (57)	73 (33%)	71 (97%)
[20-40[	422 (115)	144 (34%)	140 (97%)
[40-60[	663 (194)	191 (29%)	187 (98%)
[60-80[	399 (100)	127 (32%)	125 (98%)
[80-100[	523 (145)	169 (32%)	163 (96%)
[100-]	1025 (161)	464 (45%)	444 (96%)

Figure 24: QCI 1225 [%Completed_preop_RT] (process): Proportion of cStage II-III patients treated with a long course of preoperative pelvic RT or chemoradiation within the planned timing.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

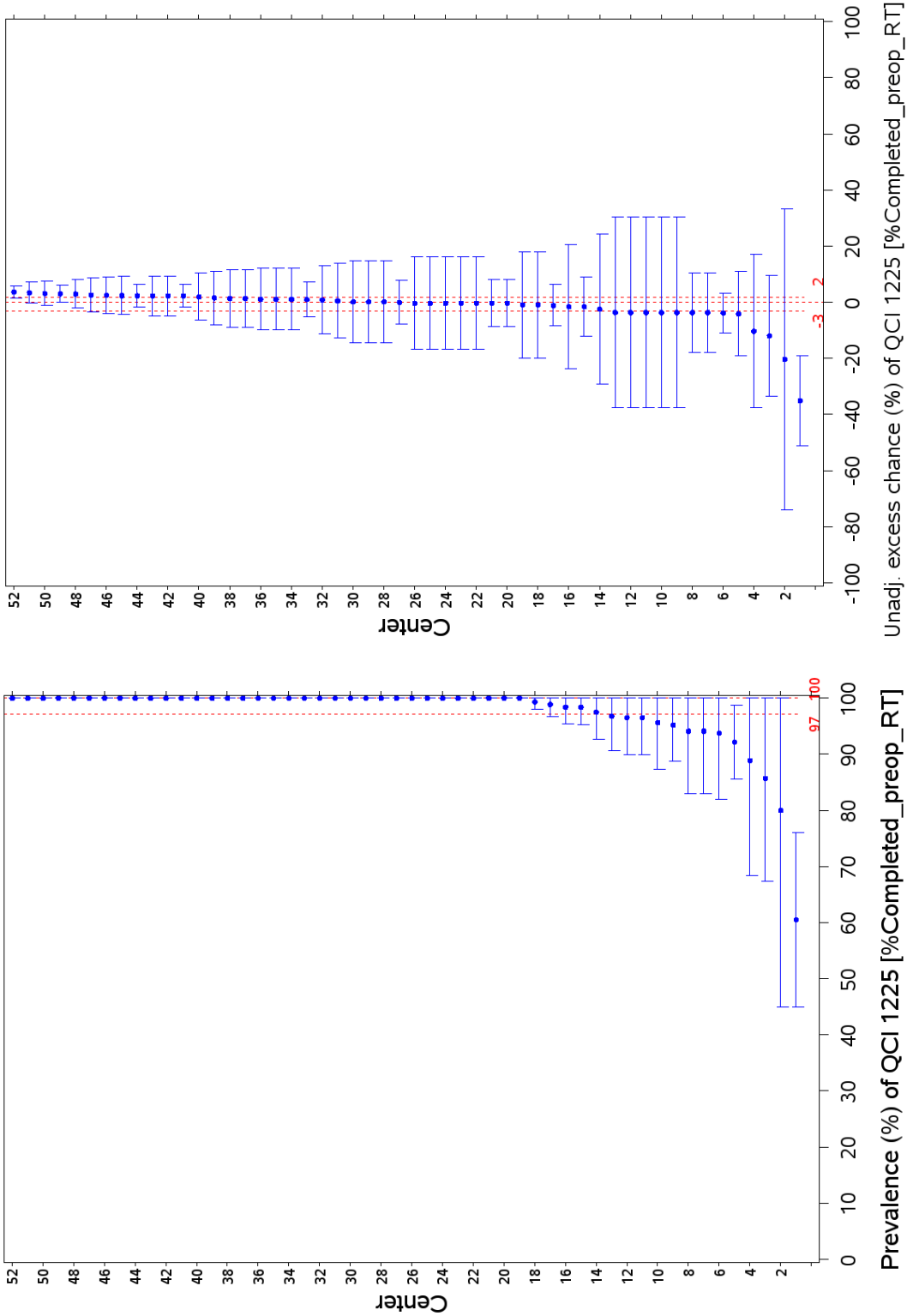


Table 35: QCI 1226 [%Surg<12w_after_Preop_RT] (process): Proportion of cStage II-III patients that was operated 4 to 12 weeks after completion of a long course of pelvic RT or chemoradiation. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (1792)	1123 (34%)	1094 (97%)
[1-10[	68 (39)	25 (37%)	25 (100%)
[10-20[	218 (126)	73 (33%)	72 (99%)
[20-40[	422 (267)	123 (29%)	119 (97%)
[40-60[	663 (409)	179 (27%)	173 (97%)
[60-80[	399 (222)	122 (31%)	121 (99%)
[80-100[	523 (318)	157 (30%)	156 (99%)
[100-]	1025 (411)	444 (43%)	428 (96%)

Figure 25: QCI 1226 [%Surg<12w_after_Preop_RT] (process): Proportion of cStage II-III patients that was operated 4 to 12 weeks after completion of a long course of pelvic RT or chemoradiation. Above: Unadj. excess probability (%), relative to the average center. Below: Prevalence (%) among eligible cases.

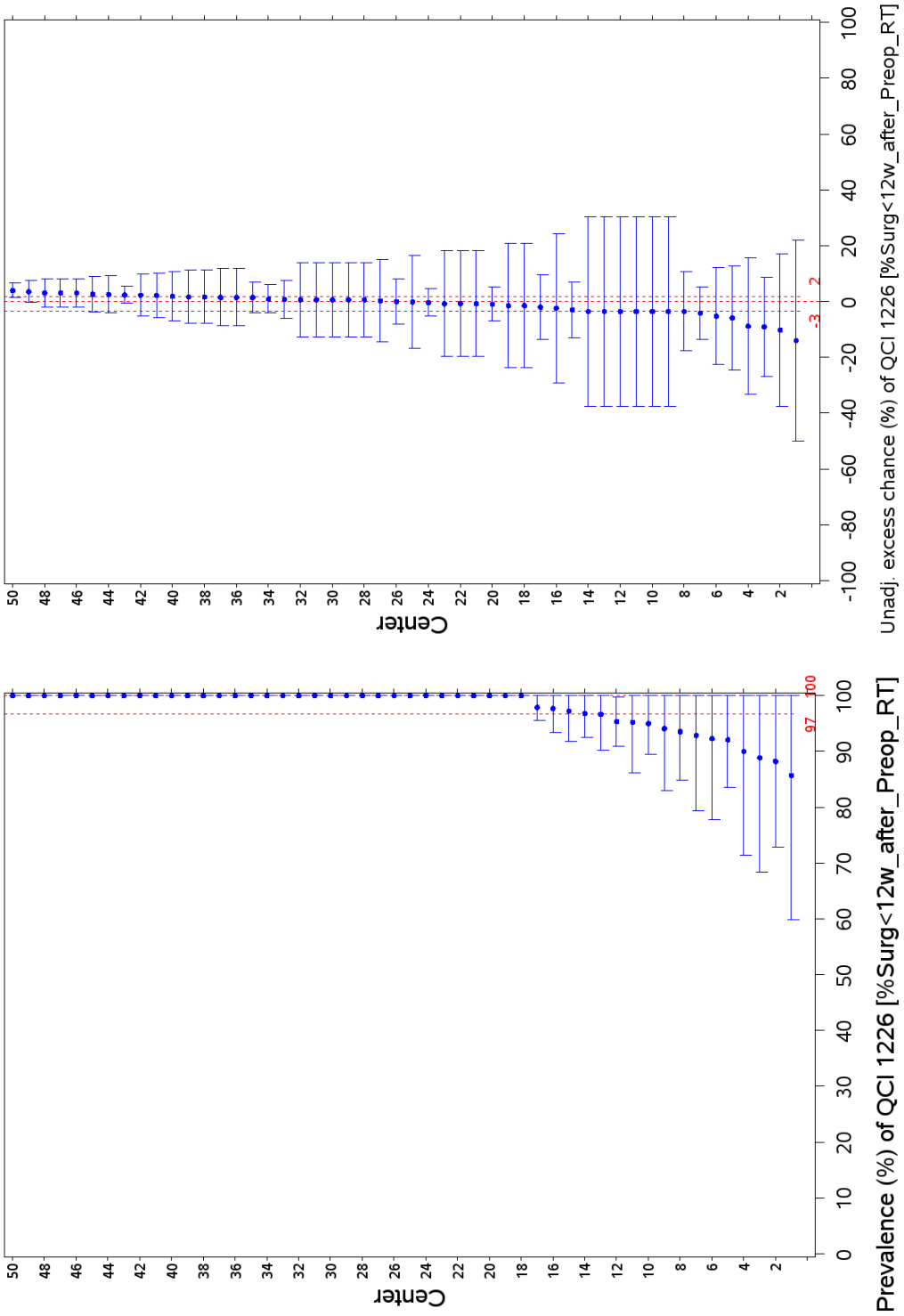


Table 36: QCI 1227 [%grade4_Tox_Preop_RT] (outcome): Rate of acute grade 4 radio(chemo)therapy-related complications. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (2774)	544 (16%)	62 (11%)
[1-10[	68 (51)	17 (25%)	3 (18%)
[10-20[	218 (184)	34 (16%)	2 (6%)
[20-40[	422 (348)	74 (18%)	11 (15%)
[40-60[	663 (554)	109 (16%)	15 (14%)
[60-80[	399 (342)	57 (14%)	6 (11%)
[80-100[	523 (433)	90 (17%)	7 (8%)
[100-]	1025 (862)	163 (16%)	18 (11%)

Figure 26: Rate of acute grade 4 radio(chemo)therapy-related complications, prevalence (%) among eligible cases

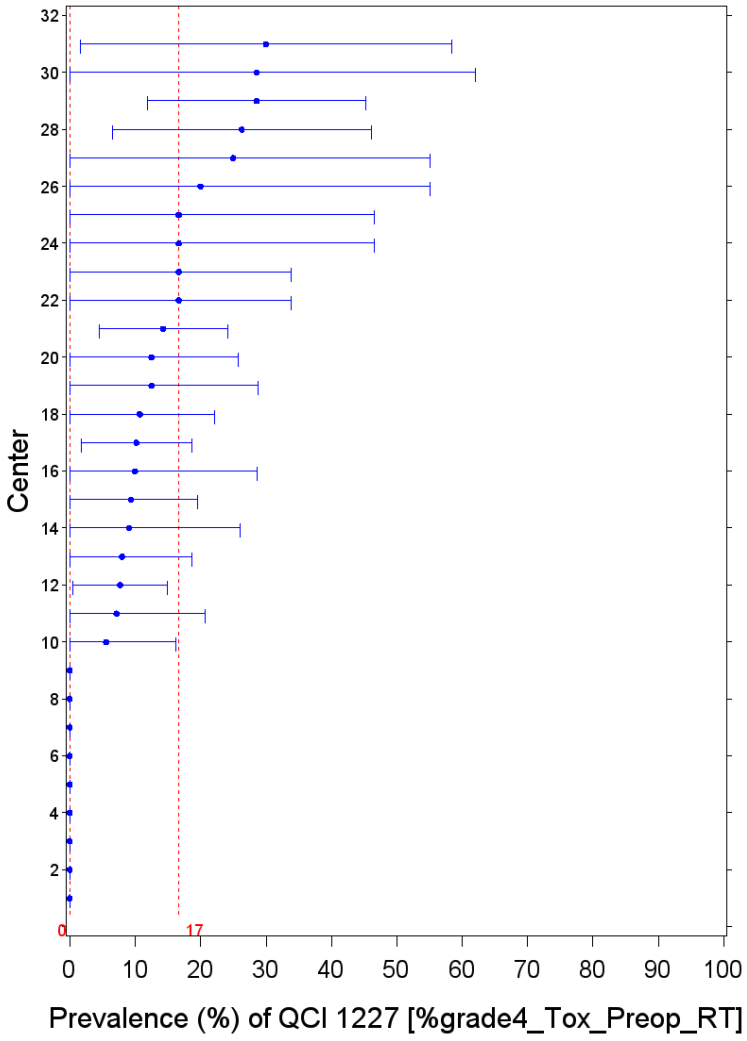
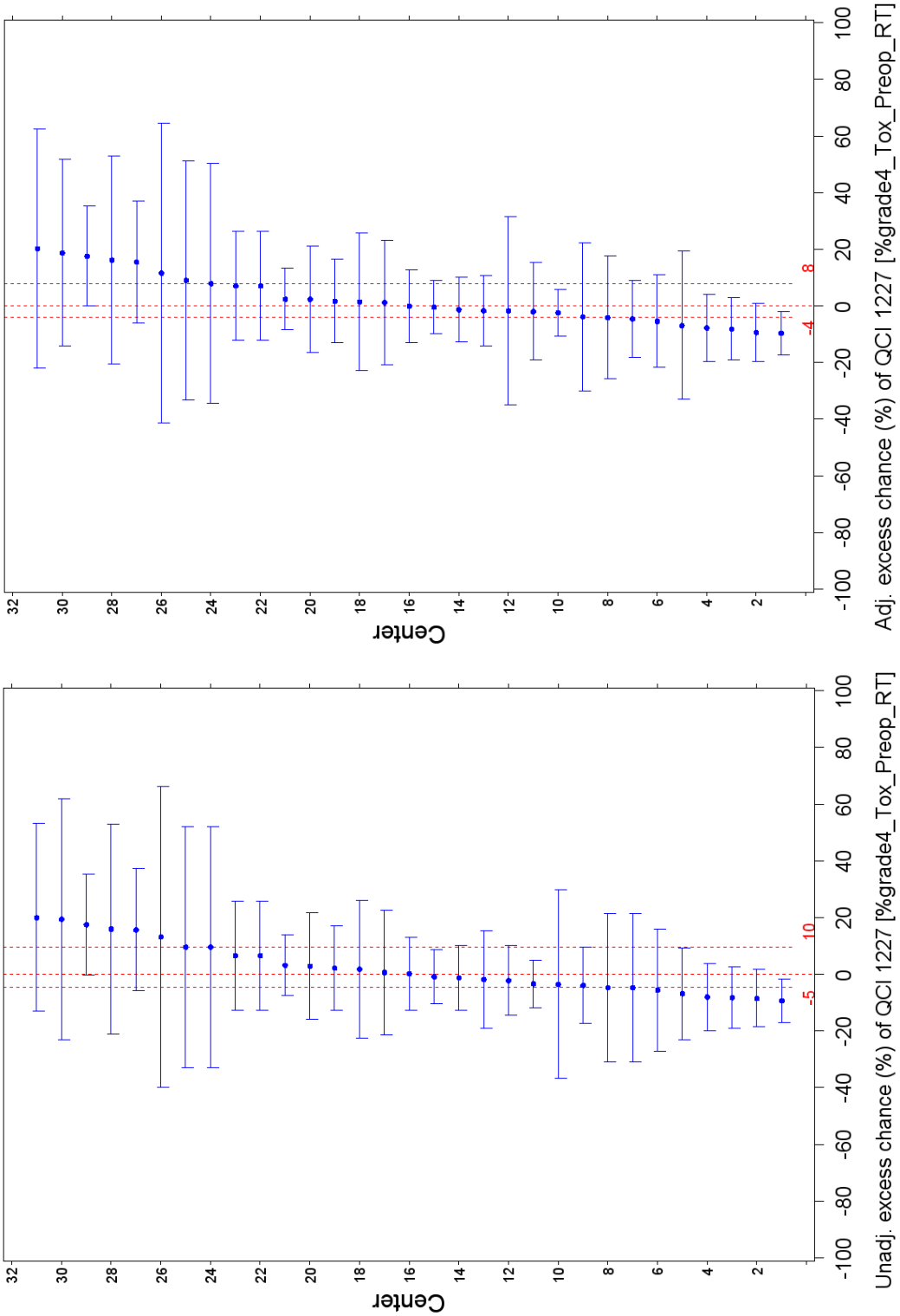


Figure 27: QCI 1227 [%grade4_Tox_Preop_RT] (outcome): Rate of acute grade 4 radio(chemo)therapy-related complications.
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.



1.5 QUALITY INDICATORS RELATED TO SURGERY

Table 37: QCI 1231 [%R0res] (outcome): Proportion of R0 resections Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (366)	2576 (78%)	2230 (87%)
[1-10[	68 (8)	54 (79%)	45 (83%)
[10-20[	218 (36)	155 (71%)	140 (90%)
[20-40[	422 (40)	324 (77%)	274 (85%)
[40-60[	663 (68)	516 (78%)	442 (86%)
[60-80[	399 (55)	308 (77%)	254 (82%)
[80-100[	523 (92)	385 (74%)	333 (86%)
[100-]	1025 (67)	834 (81%)	742 (89%)

Figure 28: QCI 1231 [%R0res] (outcome): Proportion of R0 resections, prevalence (%) among eligible cases

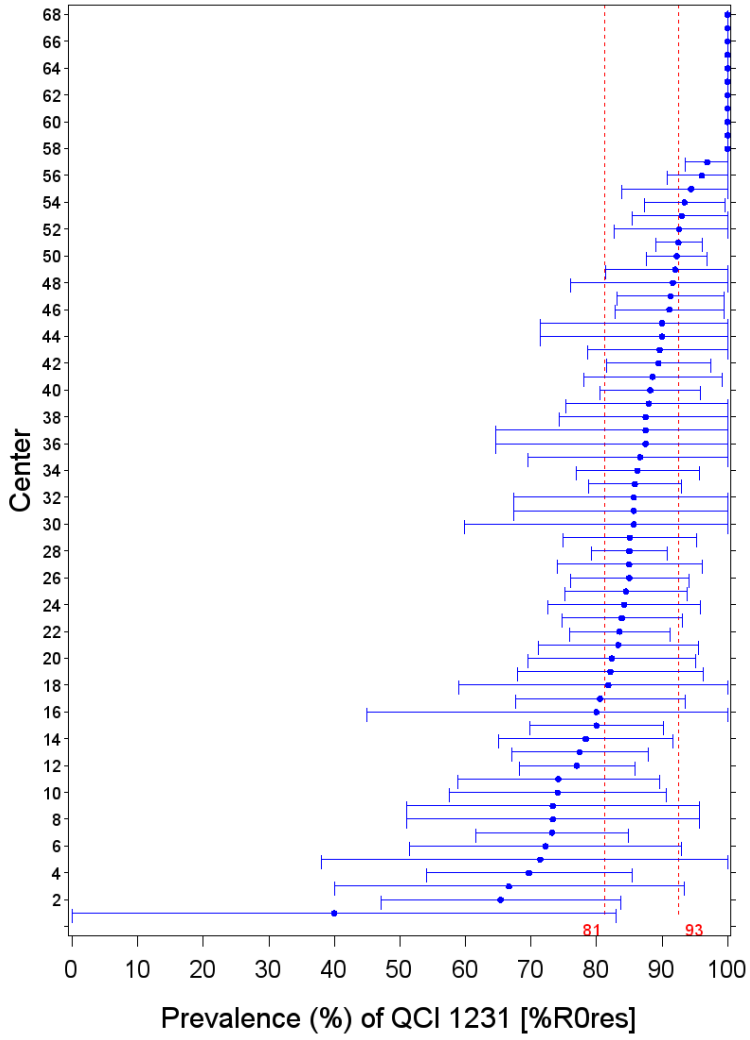


Figure 29: QCI 1231 [%R0res] (outcome): Proportion of R0 resections.
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.

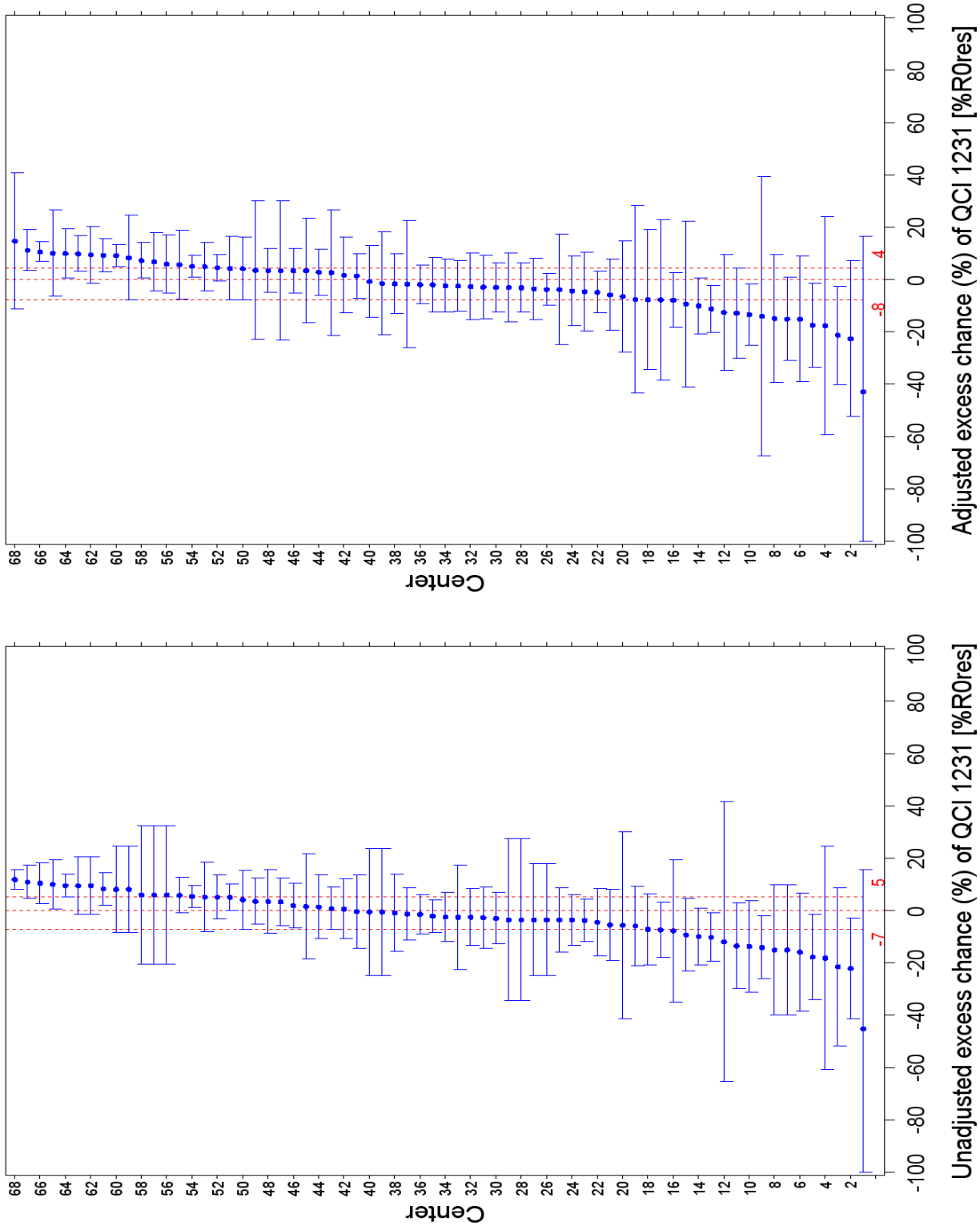
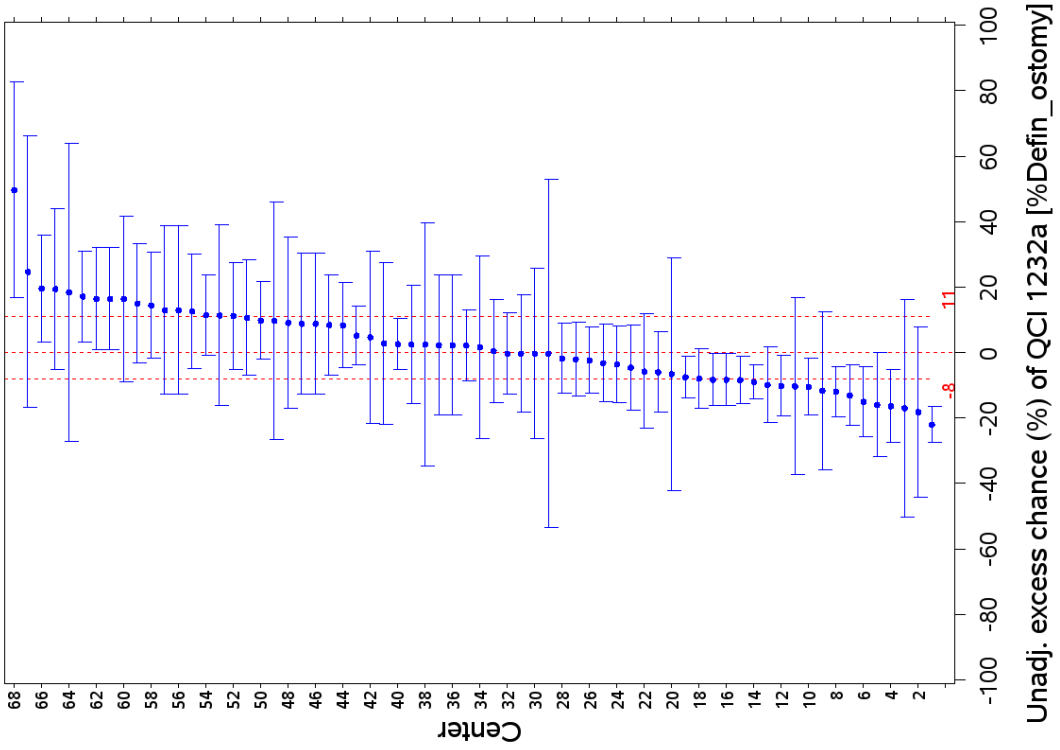


Table 38: QCI 1232a [%Defin_ostomy] (process): Proportion of APER, Hartmann's procedure or total excision of colon and rectum with definitive ileostomy.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (157)	2945 (89%)	703 (24%)
[1-10[	68 (6)	59 (87%)	18 (31%)
[10-20[	218 (5)	181 (83%)	47 (26%)
[20-40[	422 (18)	381 (90%)	122 (32%)
[40-60[	663 (36)	595 (90%)	152 (26%)
[60-80[	399 (10)	343 (86%)	91 (27%)
[80-100[	523 (48)	429 (82%)	85 (20%)
[100-]	1025 (34)	957 (93%)	188 (20%)

Figure 30: QCI 1232a [%Defin_ostomy] (process): Proportion of APER, Hartmann's procedure or total excision of colon and rectum with definitive ileostomy.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.



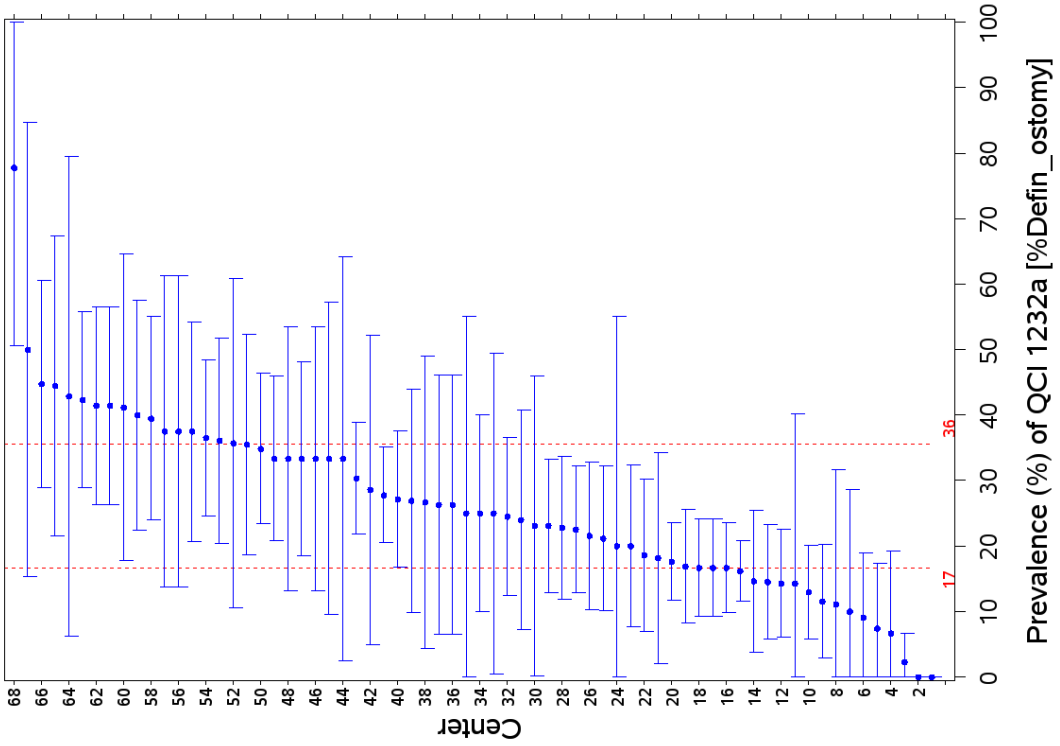


Table 39: QCI 1232b [%stoma1year] (outcome): Proportion of patients with stoma 1 year after sphincter-sparing surgery Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (3188)	123 (4%)	33 (27%)
[1-10[	68 (66)	2 (3%)	2 (100%)
[10-20[	218 (210)	7 (3%)	3 (43%)
[20-40[	422 (404)	18 (4%)	5 (28%)
[40-60[	663 (637)	25 (4%)	2 (8%)
[60-80[	399 (383)	15 (4%)	4 (27%)
[80-100[	523 (506)	17 (3%)	6 (35%)
[100-]	1025 (982)	39 (4%)	11 (28%)

Figure 31: QCI 1232b [%stoma1year] (outcome): Proportion of patients with stoma 1 year after sphincter-sparing surgery, prevalence (%) among eligible cases

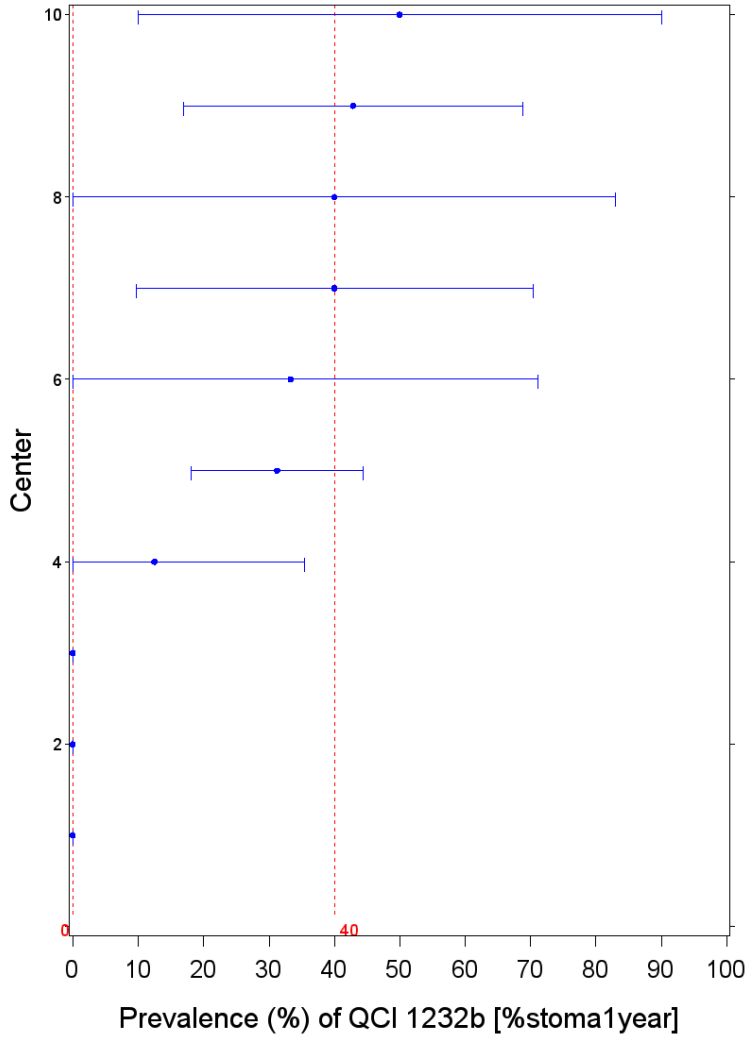


Figure 32: QCI 1232b [%stoma1year] (outcome): Proportion of patients with stoma 1 year after sphincter-sparing surgery
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.

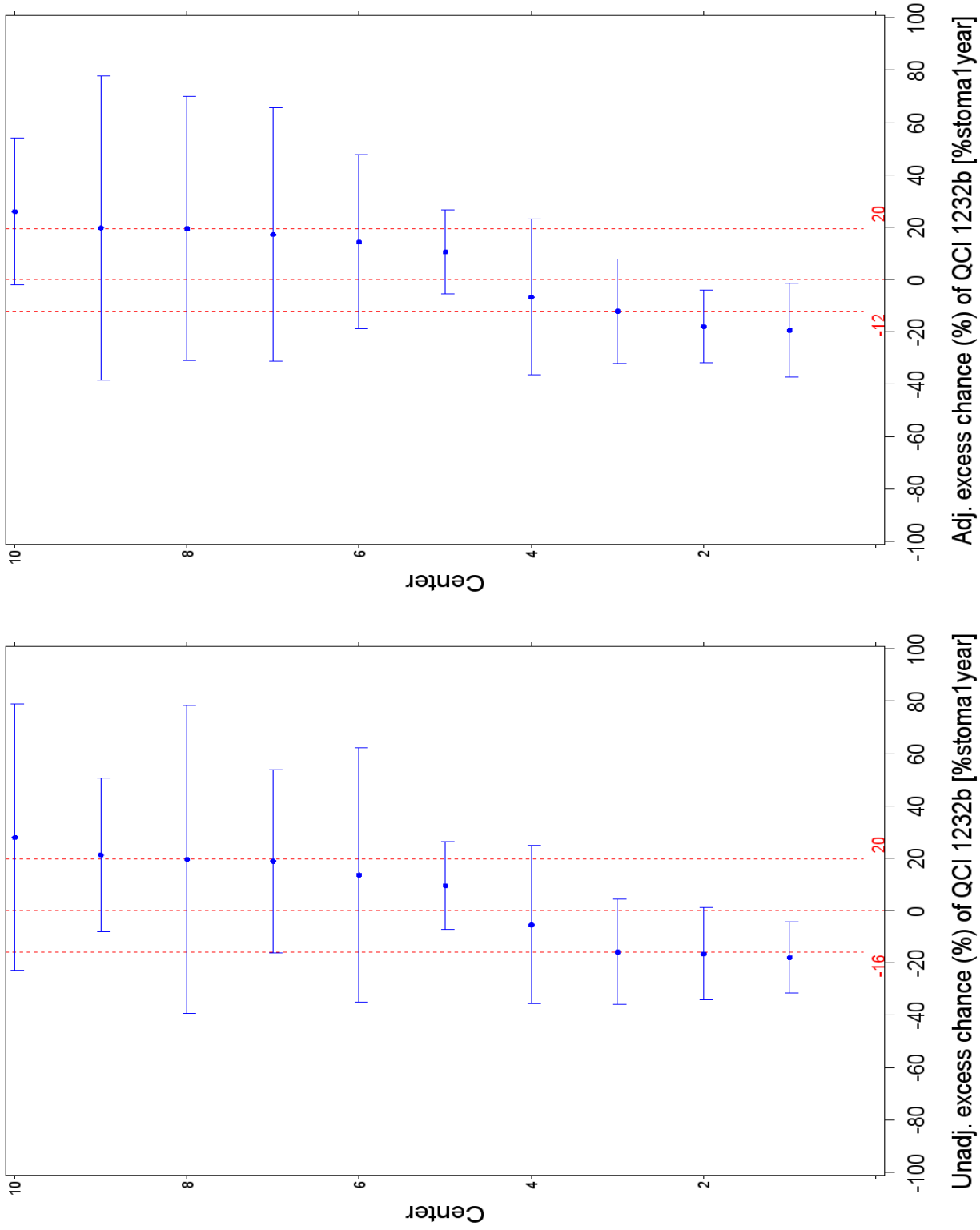


Table 40: QCI 1233a [%Leak_PME] (outcome): Major leakage after PME + SSO + reconstruction
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (385)	556 (17%)	32 (6%)
[1-10[	68 (9)	7 (10%)	0 (0%)
[10-20[	218 (40)	56 (26%)	4 (7%)
[20-40[	422 (42)	73 (17%)	7 (10%)
[40-60[	663 (69)	169 (25%)	7 (4%)
[60-80[	399 (61)	44 (11%)	3 (7%)
[80-100[	523 (93)	78 (15%)	6 (8%)
[100-]	1025 (71)	129 (13%)	5 (4%)

Figure 33: QCI 1233a [%Leak_PME] (outcome): Major leakage after PME + SSO + reconstruction, prevalence (%) among eligible cases

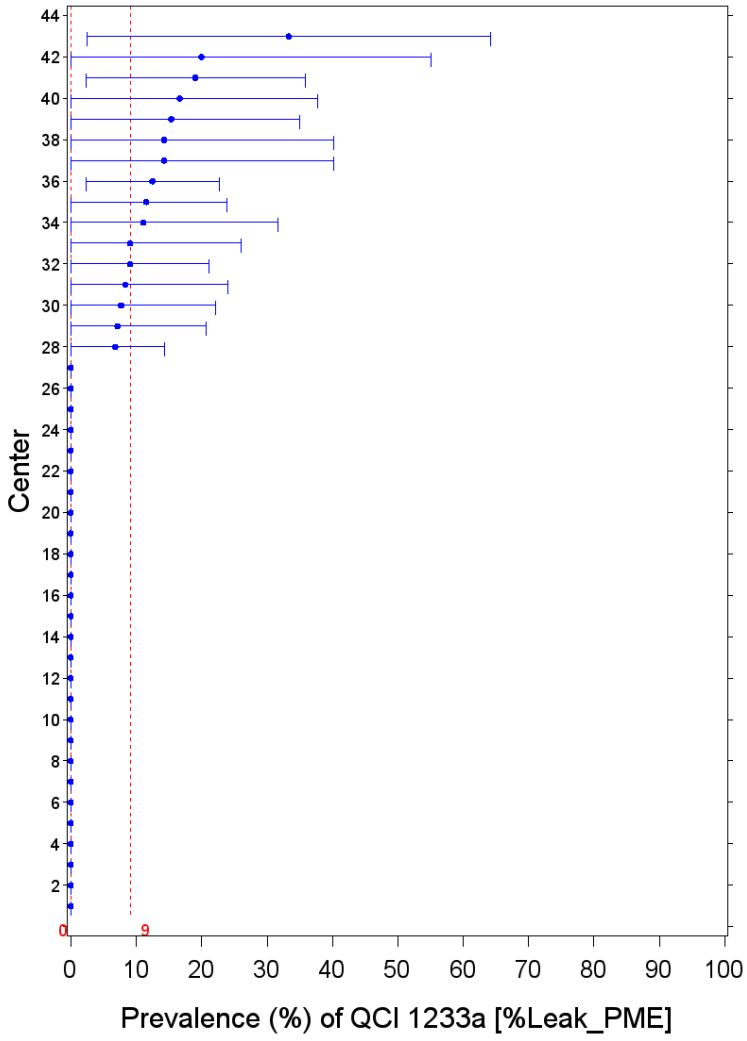


Figure 34: QCI 1233a [%Leak_PME] (outcome): Major leakage after PME + SSO + reconstruction
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.

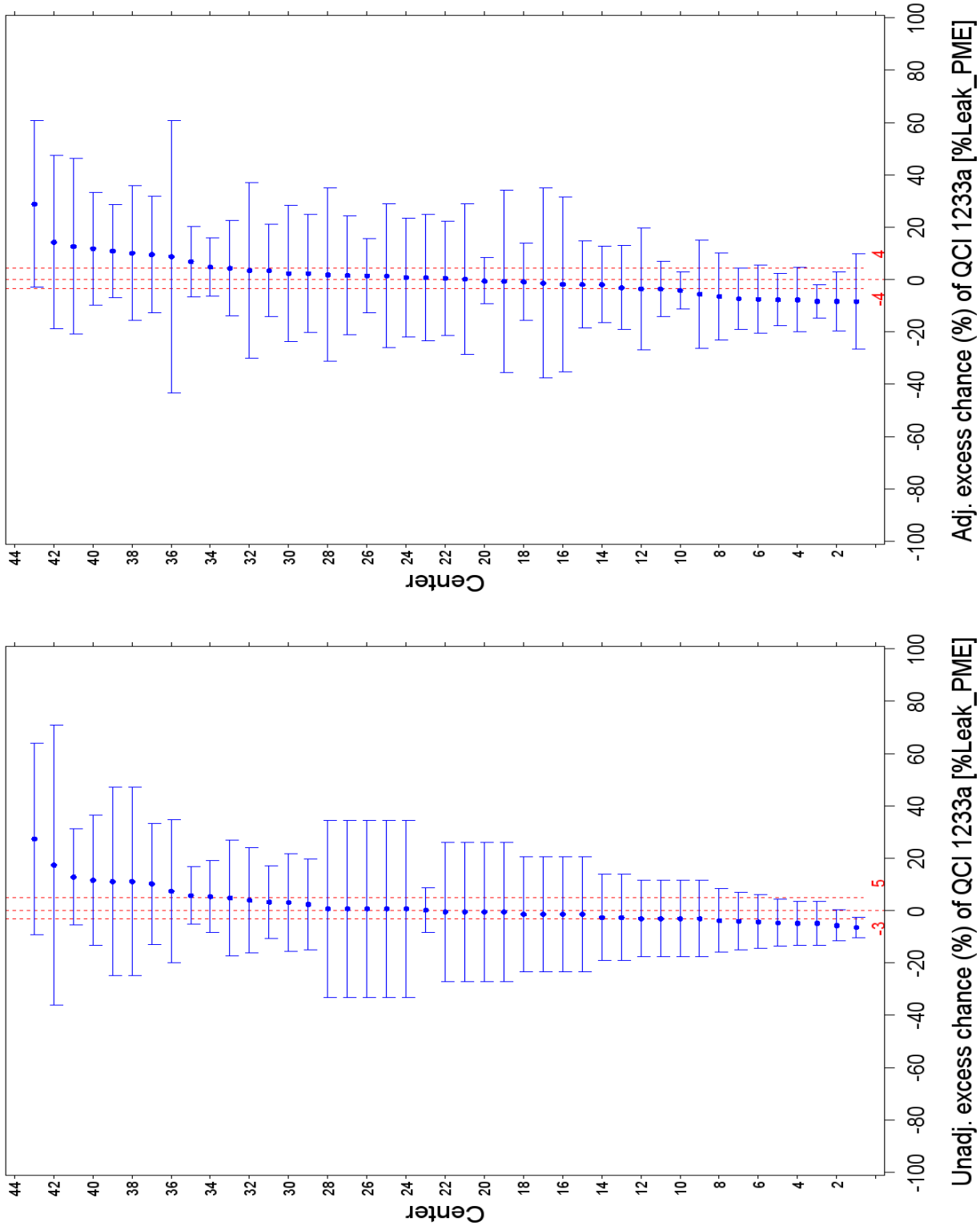


Table 41: QCI 1233b [%Leak_TME] (outcome): Major leakage after TME + SSO + reconstruction
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (385)	1592 (48%)	97 (6%)
[1-10[	68 (9)	34 (50%)	1 (3%)
[10-20[	218 (40)	72 (33%)	6 (8%)
[20-40[	422 (42)	174 (41%)	11 (6%)
[40-60[	663 (69)	254 (38%)	17 (7%)
[60-80[	399 (61)	199 (50%)	15 (8%)
[80-100[	523 (93)	253 (48%)	12 (5%)
[100-]	1025 (71)	606 (59%)	35 (6%)

Figure 35: QCI 1233b [%Leak_TME] (outcome): Major leakage after TME + SSO + reconstruction, prevalence (%) among eligible cases

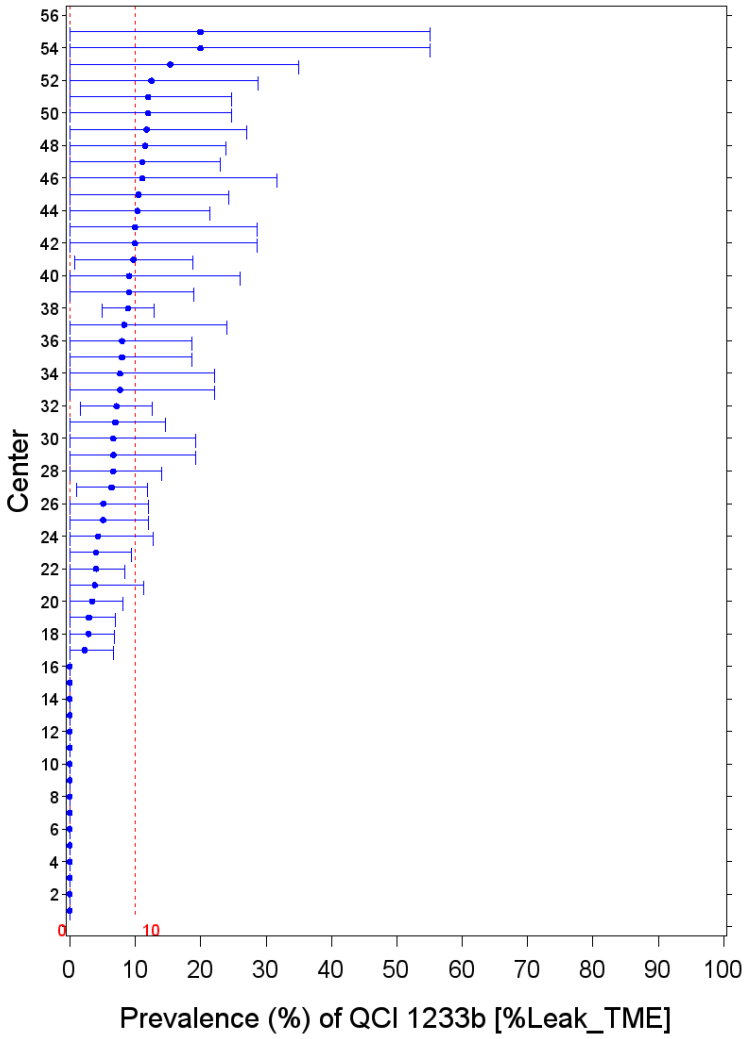


Figure 36: QCI 1233b [%Leak_TME] (outcome): Major leakage after TME + SSO + reconstruction
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.

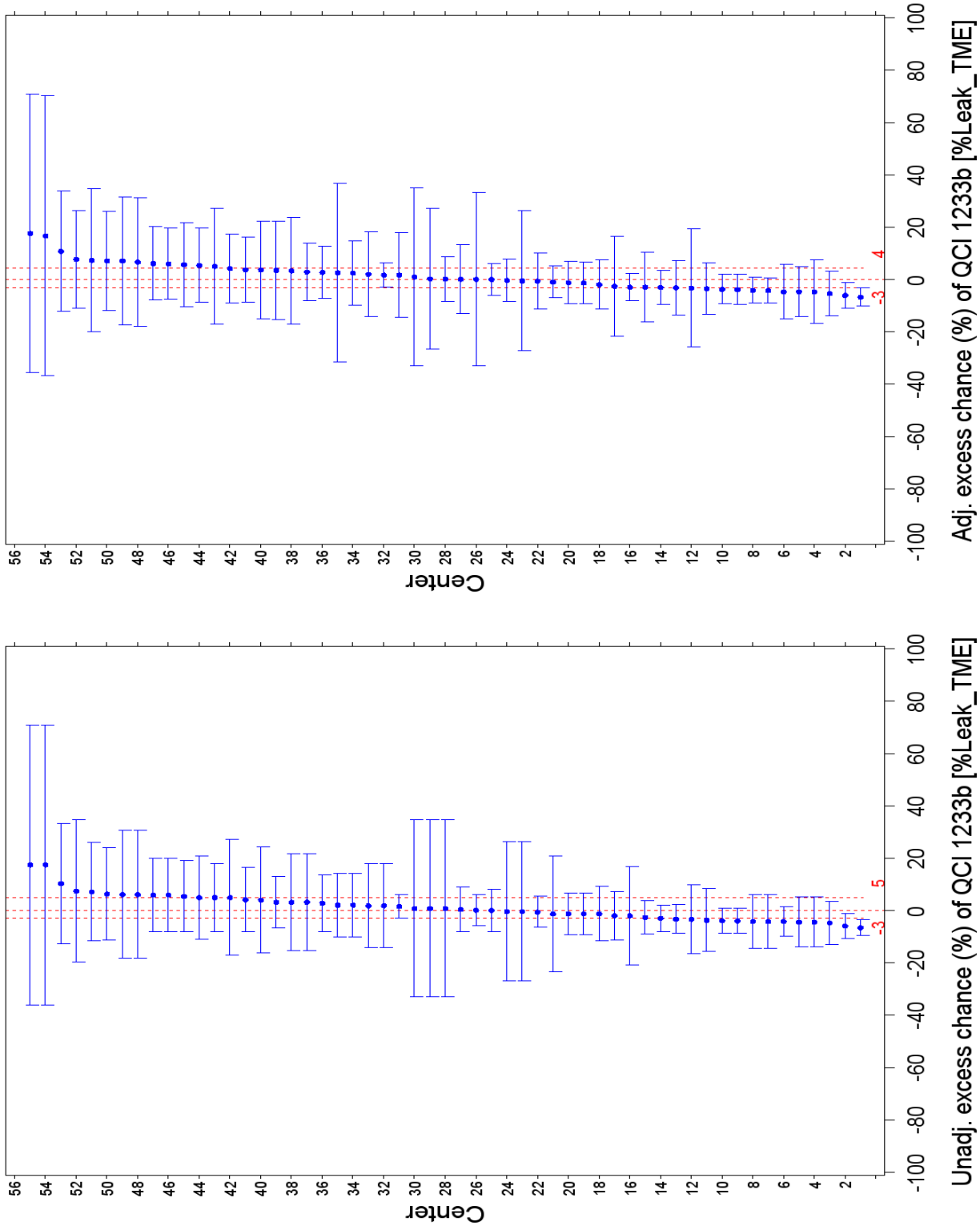


**Table 42: QCI 1234 [30d_mort] (outcome): Inpatient or 30-day mortality after radical surgical resection
Missingness, eligibility and prevalence information.**

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (361)	2919 (88%)	50 (2%)
[1-10[	68 (9)	59 (87%)	1 (2%)
[10-20[	218 (35)	181 (83%)	5 (3%)
[20-40[	422 (38)	382 (91%)	9 (2%)
[40-60[	663 (65)	587 (89%)	8 (1%)
[60-80[	399 (54)	345 (86%)	14 (4%)
[80-100[	523 (90)	424 (81%)	8 (2%)
[100-]	1025 (70)	941 (92%)	5 (1%)

Figure 37: QCI 1234 [30d_mort] (outcome): Inpatient or 30-day mortality after radical surgical resection, prevalence (%) among eligible cases

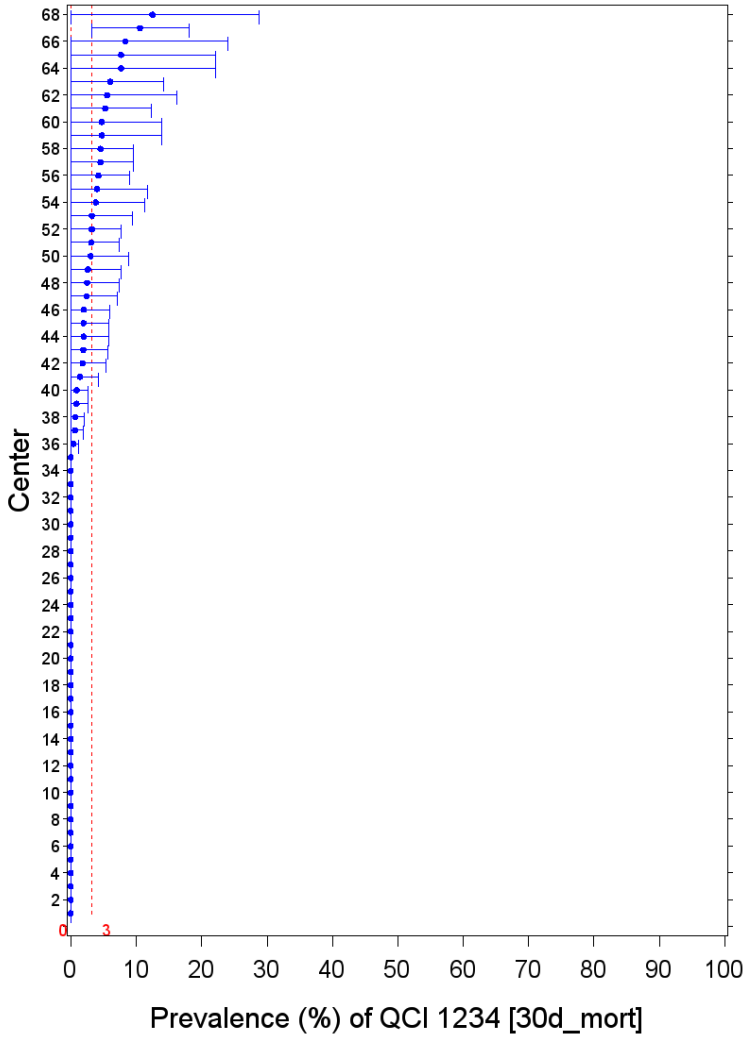


Figure 38: QCI 1234 [30d_mort] (outcome): Inpatient or 30-day mortality after radical surgical resection
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.

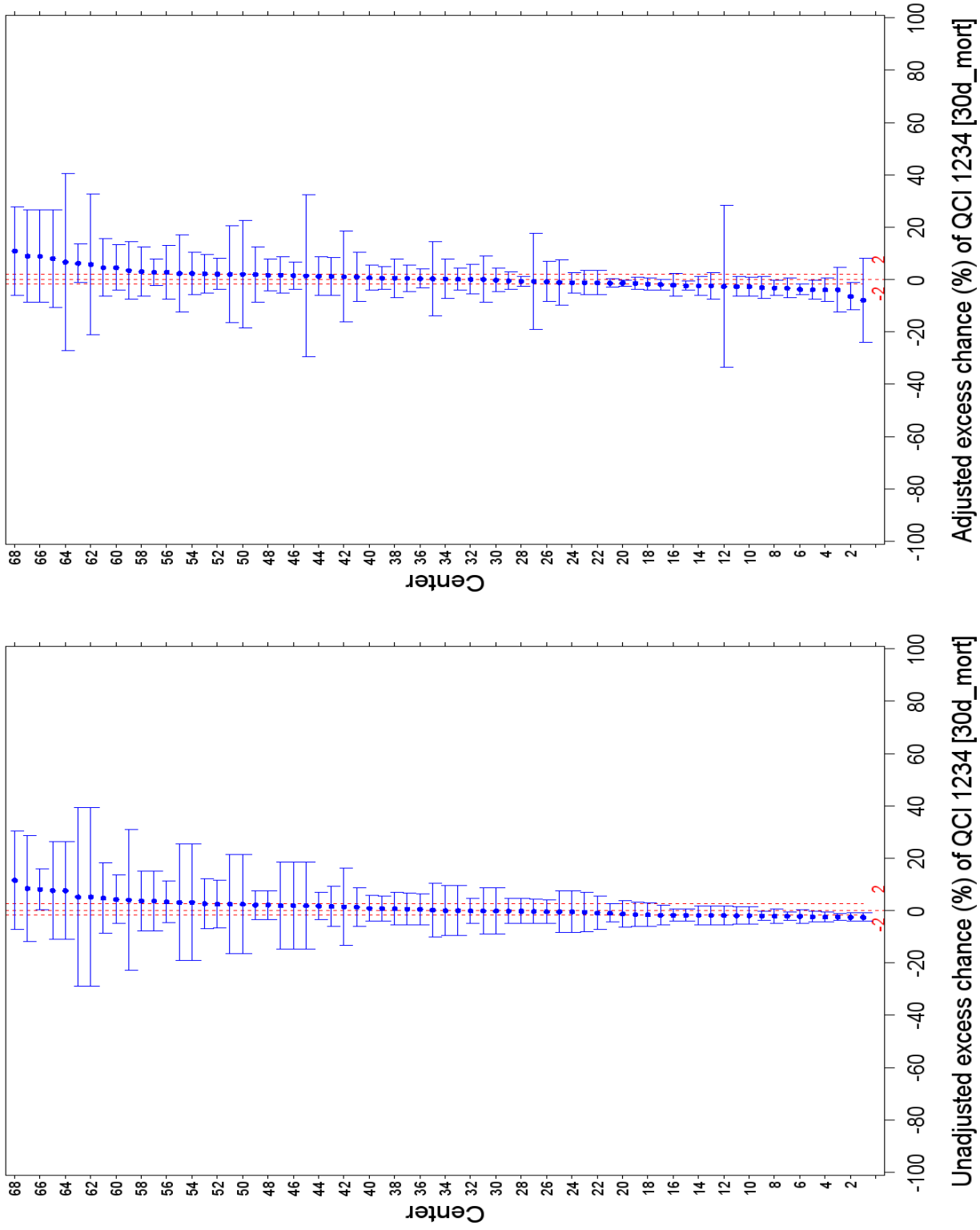


Table 43: QCI 1234b [%Major_morb] (outcome): Postoperative major surgical morbidity with reintervention under narcosis after radical surgical resection
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (369)	2913 (88%)	167 (6%)
[1-10[	68 (8)	60 (88%)	1 (2%)
[10-20[	218 (40)	176 (81%)	11 (6%)
[20-40[	422 (39)	381 (90%)	28 (7%)
[40-60[	663 (66)	587 (89%)	30 (5%)
[60-80[	399 (58)	341 (85%)	23 (7%)
[80-100[	523 (91)	424 (81%)	25 (6%)
[100-]	1025 (67)	944 (92%)	49 (5%)

Figure 39: QCI 1234b [%Major_morb] (outcome): Postoperative major surgical morbidity with reintervention under narcosis after radical surgical resection, prevalence (%) among eligible cases

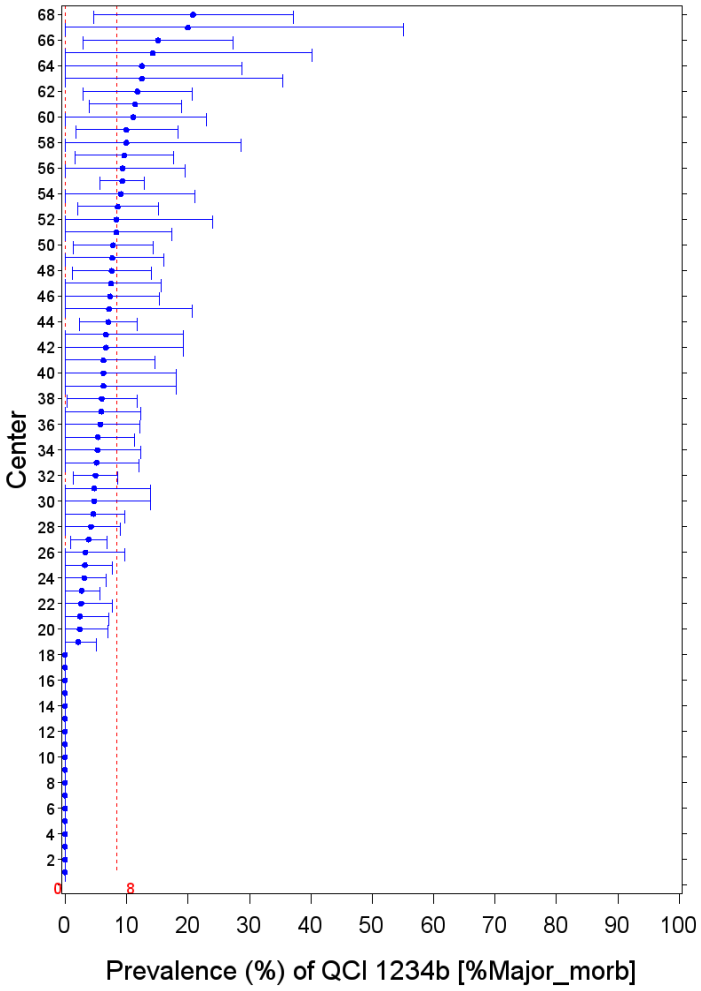


Figure 40: QCI 1234b [%Major_morb] (outcome): Postoperative major surgical morbidity with reintervention under narcosis after radical surgical resection.
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.

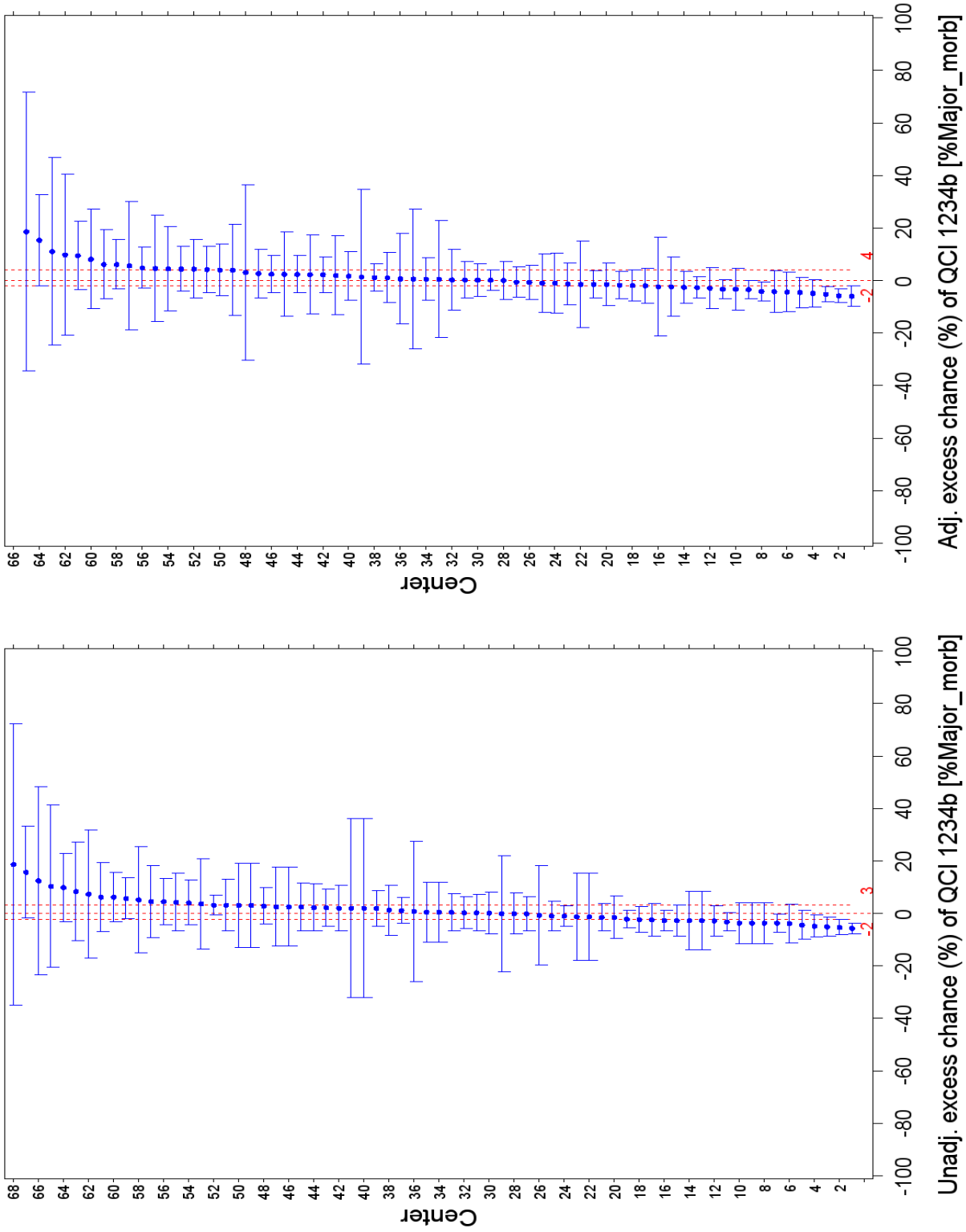


Table 44: QCI 1235 [%Perfor] (outcome): Rate of intra-operative rectal perforation
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (380)	2900 (87%)	220 (8%)
[1-10[	68 (8)	60 (88%)	3 (5%)
[10-20[	218 (35)	181 (83%)	14 (8%)
[20-40[	422 (37)	383 (91%)	35 (9%)
[40-60[	663 (68)	584 (88%)	52 (9%)
[60-80[	399 (53)	346 (87%)	35 (10%)
[80-100[	523 (90)	424 (81%)	24 (6%)
[100-]	1025 (89)	922 (90%)	57 (6%)

Figure 41: QCI 1235 [%Perfor] (outcome): Rate of intra-operative rectal perforation, prevalence (%) among eligible cases

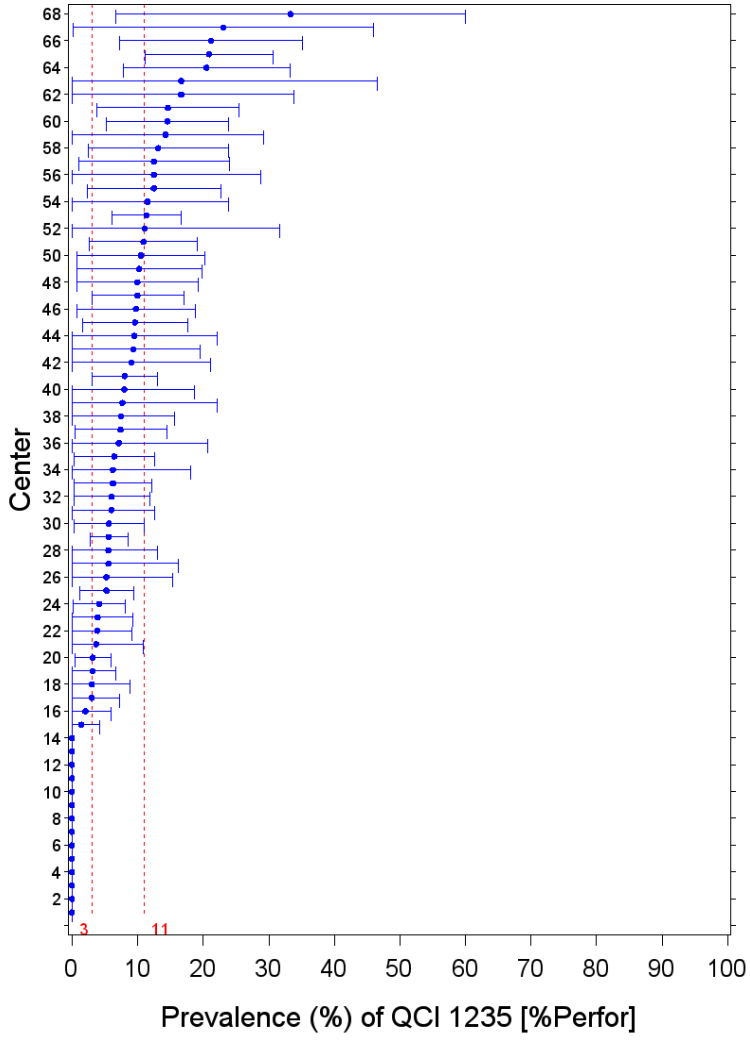
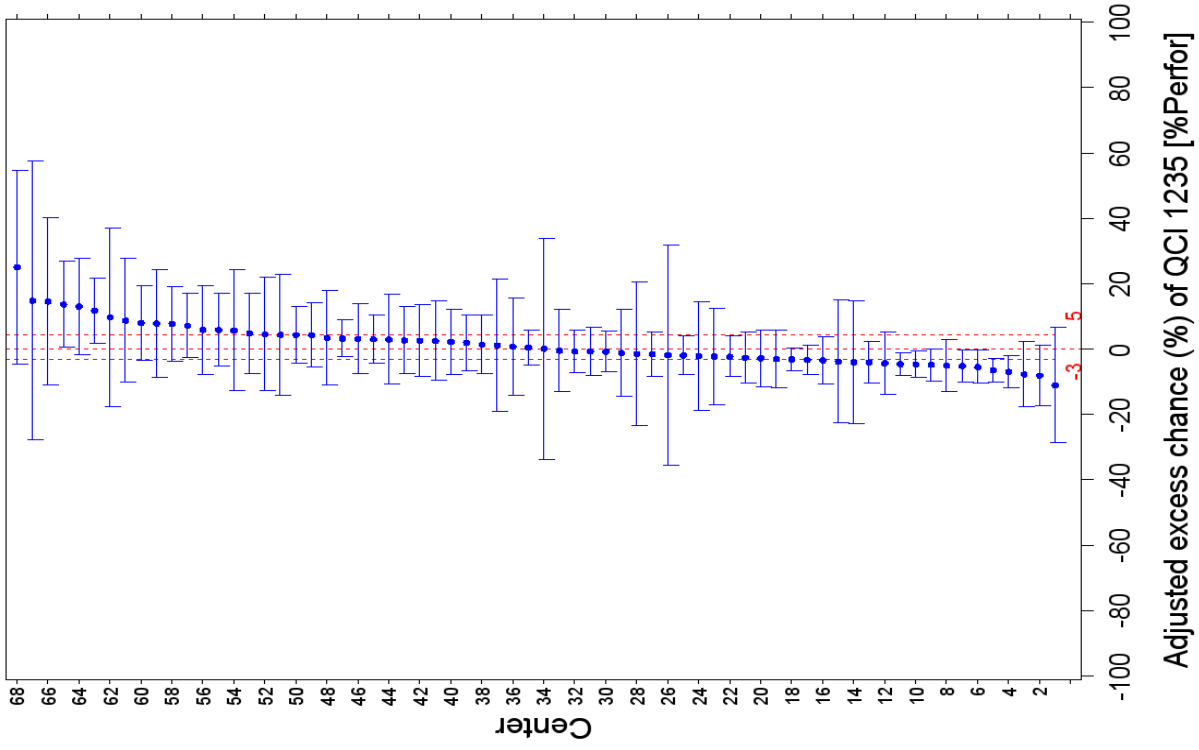


Figure 42: QCI 1235 [%Perfor] (outcome): Rate of intra-operative rectal perforation
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.



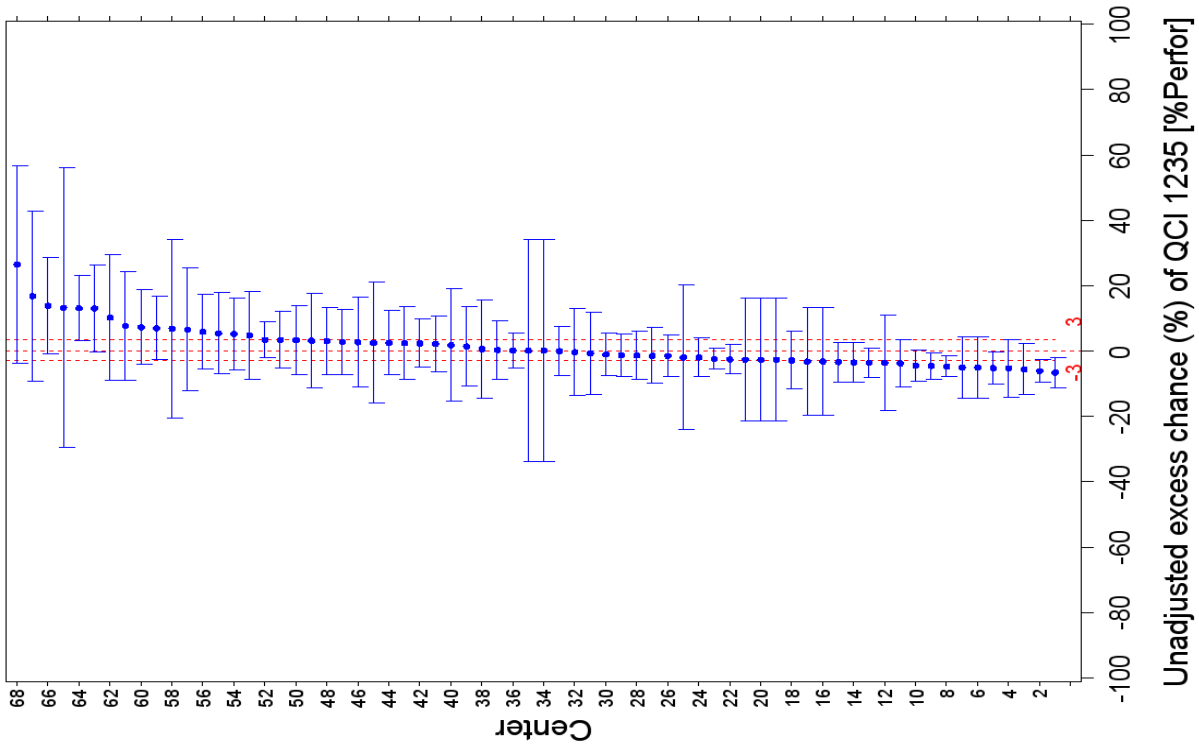


Table 45: QCI 1235b [%Pos_Dist_margin] (outcome): (y)p Distal margin involved (positive) after SSO or Hartmann for low rectal cancer (= 5 cm)
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (692)	516 (16%)	9 (2%)
[1-10[	68 (13)	12 (18%)	0 (0%)
[10-20[	218 (88)	19 (9%)	0 (0%)
[20-40[	422 (82)	45 (11%)	2 (4%)
[40-60[	663 (139)	77 (12%)	3 (4%)
[60-80[	399 (79)	62 (16%)	1 (2%)
[80-100[	523 (169)	78 (15%)	1 (1%)
[100-]	1025 (122)	223 (22%)	2 (1%)

Figure 43: QCI 1235b [%Pos_Dist_margin] (outcome): (y)p Distal margin involved (positive) after SSO or Hartmann for low rectal cancer (= 5 cm), prevalence (%) among eligible cases

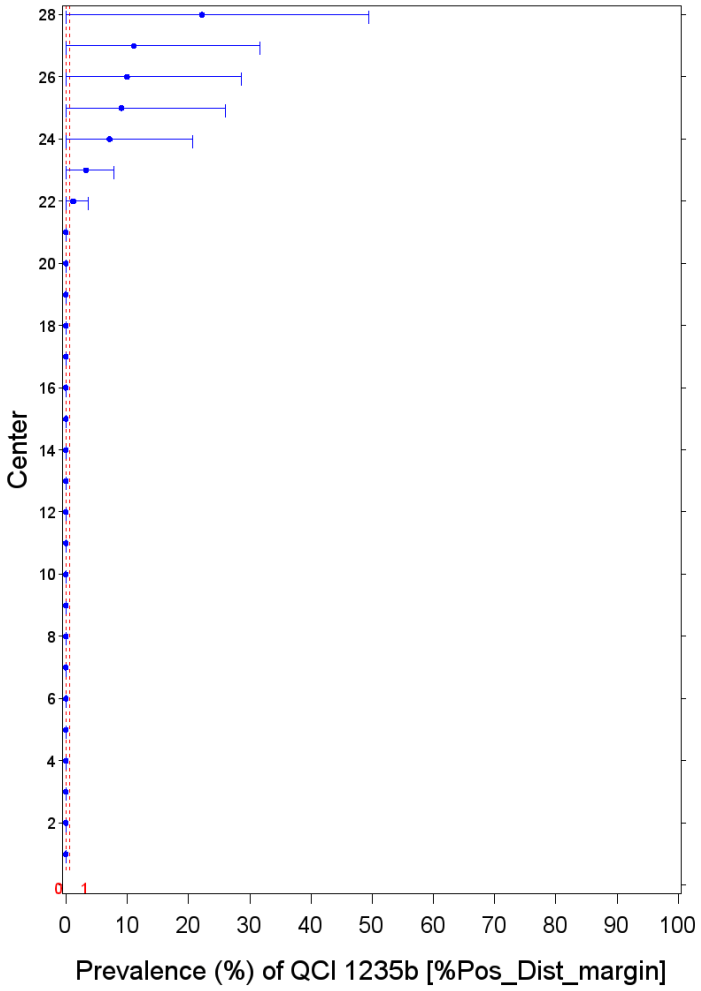


Figure 44: QCI 1235b [%Pos_Dist_margin] (outcome): (y)p Distal margin involved (positive) after SSO or Hartmann for low rectal cancer (= 5 cm)
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.

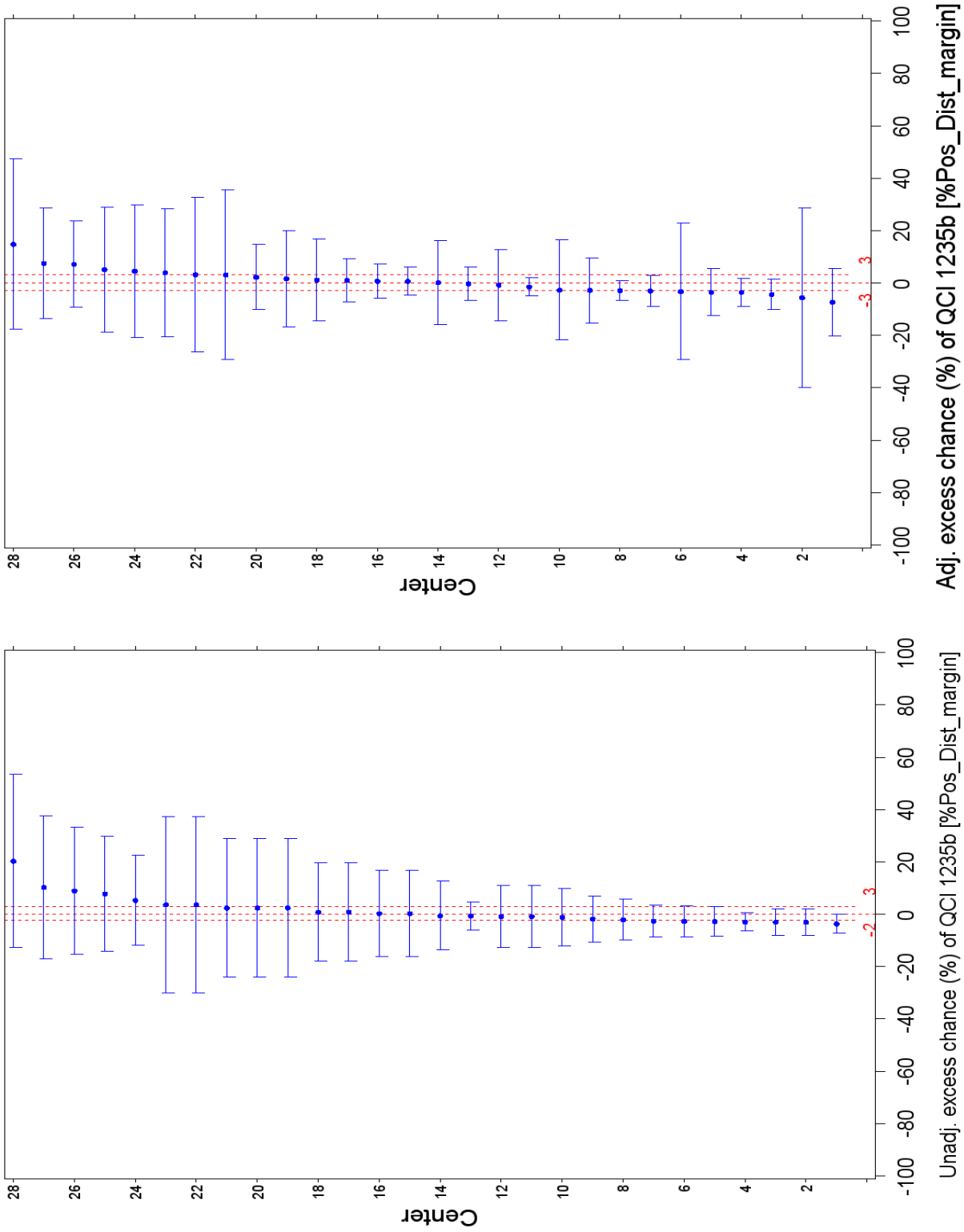


Table 46: QCI 1235c [%Pos_CRM] (outcome): Mesorectal (y)pCRM positivity after radical surgical resection
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (1286)	1932 (58%)	361 (19%)
[1-10[	68 (24)	43 (63%)	10 (23%)
[10-20[	218 (121)	90 (41%)	14 (16%)
[20-40[	422 (158)	254 (60%)	55 (22%)
[40-60[	663 (282)	366 (55%)	68 (19%)
[60-80[	399 (145)	247 (62%)	58 (23%)
[80-100[	523 (209)	290 (55%)	44 (15%)
[100-]	1025 (347)	642 (63%)	112 (17%)

Figure 45: QCI 1235c [%Pos_CRM] (outcome): Mesorectal (y)pCRM positivity after radical surgical resection, prevalence (%) among eligible cases

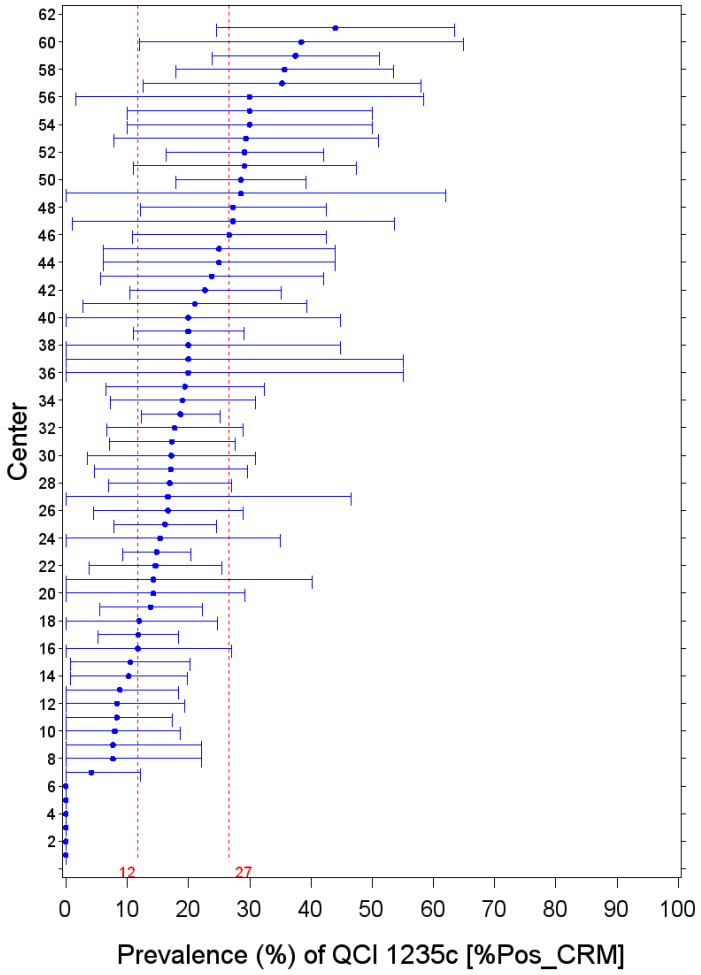
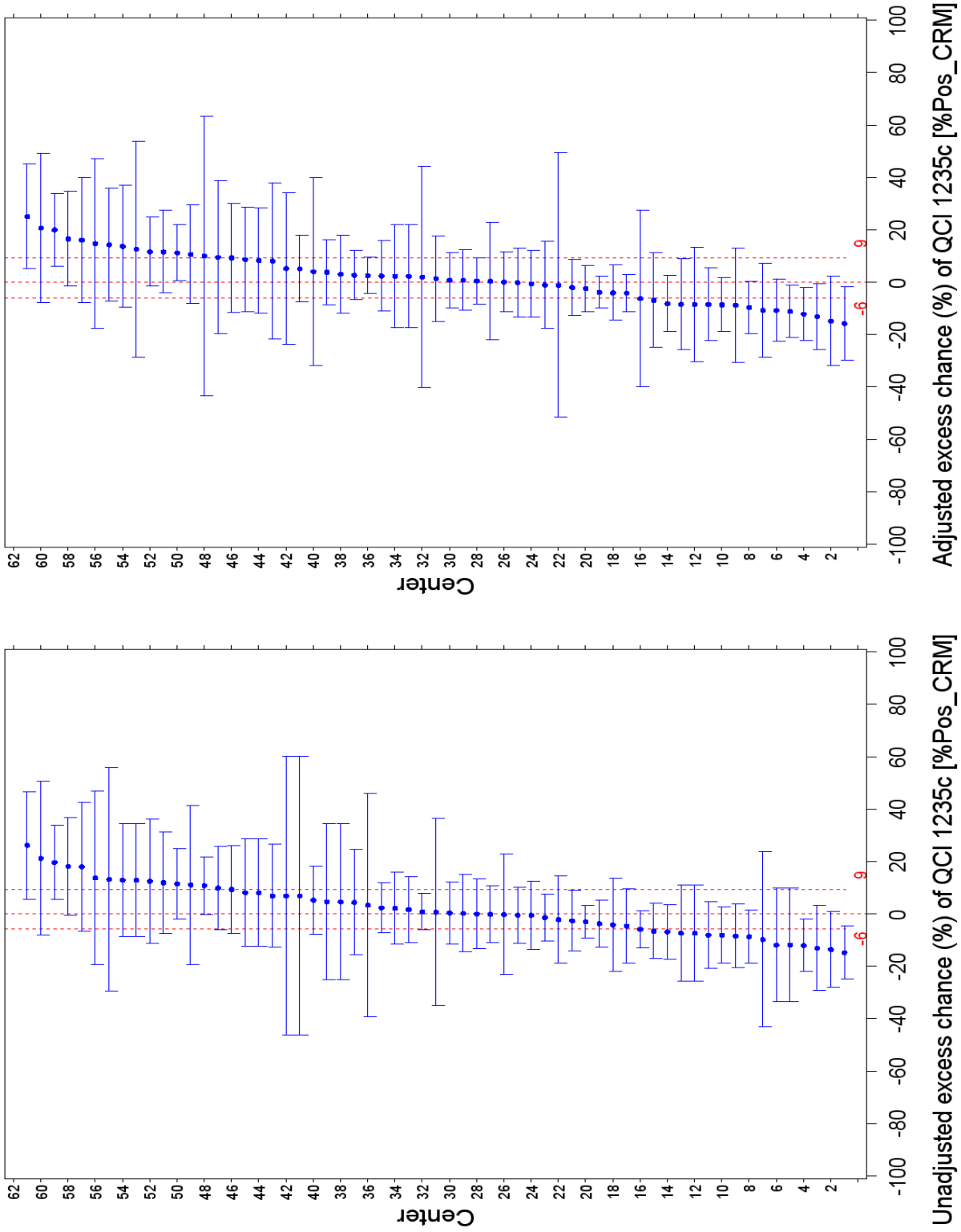


Figure 46: QCI 1235c [%Pos_CRM] (outcome): Mesorectal (y)pCRM positivity after radical surgical resection
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.



1.6 QUALITY INDICATORS RELATED TO ADJUVANT TREATMENT

Table 47: QCI 1241 [%Adj-Chemo<3m] (process): Proportion of (y)pStage III patients with R0 resection that received adjuvant chemotherapy within 3 months after surgery. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (2660)	28 (1%)	24 (86%)
[1-10[	68 (55)	0 (0%)	
[10-20[	218 (179)	2 (1%)	2 (100%)
[20-40[	422 (338)	10 (2%)	9 (90%)
[40-60[	663 (535)	4 (1%)	3 (75%)
[60-80[	399 (318)	0 (0%)	
[80-100[	523 (422)	6 (1%)	4 (67%)
[100-]	1025 (813)	6 (1%)	6 (100%)

Table 48: QCI 1242 [%Adj_RT<3m] (process): Proportion of pStage II-III patients with R0 resection that received adjuvant radiotherapy or chemoradiotherapy within 3 months after surgery. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (3242)	46 (1%)	45 (98%)
[1-10[	68 (67)	1 (1%)	1 (100%)
[10-20[	218 (214)	2 (1%)	2 (100%)
[20-40[	422 (416)	4 (1%)	4 (100%)
[40-60[	663 (647)	9 (1%)	9 (100%)
[60-80[	399 (390)	3 (1%)	3 (100%)
[80-100[	523 (508)	11 (2%)	11 (100%)
[100-]	1025 (1000)	16 (2%)	15 (94%)

Table 49: QCI 1243 [%Adj_Chemo<12w] (process): Proportion of (y)pStage II-III patients with R0 resection that started adjuvant chemotherapy for (y)pStage II or III within 12 weeks after surgery. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (126)	58 (2%)	54 (93%)
[1-10[	68 (5)	0 (0%)	
[10-20[	218 (7)	2 (1%)	2 (100%)
[20-40[	422 (18)	12 (3%)	11 (92%)
[40-60[	663 (24)	16 (2%)	15 (94%)
[60-80[	399 (13)	1 (0%)	1 (100%)
[80-100[	523 (20)	14 (3%)	12 (86%)
[100-]	1025 (39)	13 (1%)	13 (100%)

Table 50: QCI 1244 [%Adj_5FU] (process): Proportion of (y)pStage II-III patients with R0 resection treated with adjuvant chemo(radio)therapy, that received 5-FU based chemotherapy. Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (2568)	57 (2%)	54 (95%)
[1-10[	68 (45)	0 (0%)	
[10-20[	218 (173)	2 (1%)	2 (100%)
[20-40[	422 (319)	11 (3%)	11 (100%)
[40-60[	663 (514)	16 (2%)	16 (100%)
[60-80[	399 (334)	1 (0%)	1 (100%)
[80-100[	523 (392)	14 (3%)	14 (100%)
[100-]	1025 (791)	13 (1%)	10 (77%)

Table 51: QCI 1245 [%grade4_Tox_Prostop_CT] (outcome): Rate of acute grade 4 chemotherapy-related complications Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (3054)	128 (4%)	10 (8%)
[1-10[	68 (61)	3 (4%)	0 (0%)
[10-20[	218 (200)	6 (3%)	0 (0%)
[20-40[	422 (379)	26 (6%)	4 (15%)
[40-60[	663 (601)	22 (3%)	3 (14%)
[60-80[	399 (379)	7 (2%)	0 (0%)
[80-100[	523 (474)	22 (4%)	1 (5%)
[100-]	1025 (960)	42 (4%)	2 (5%)

Figure 47: QCI 1245 [%grade4_Tox_Prostop_CT] (outcome): Rate of acute grade 4 chemotherapy-related complications, prevalence (%) among eligible cases

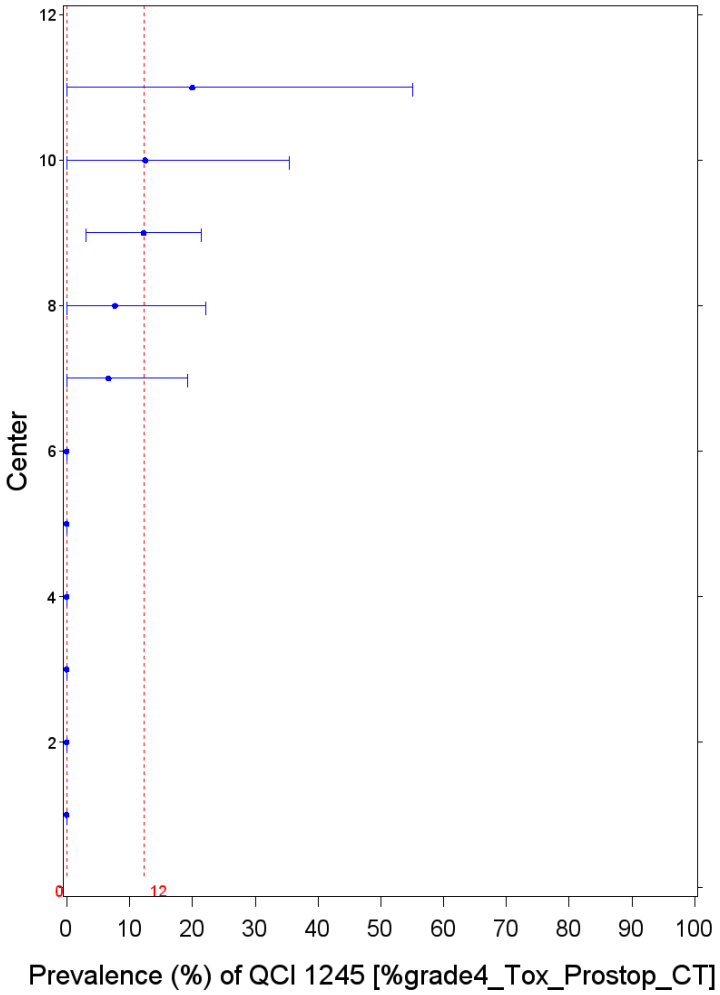
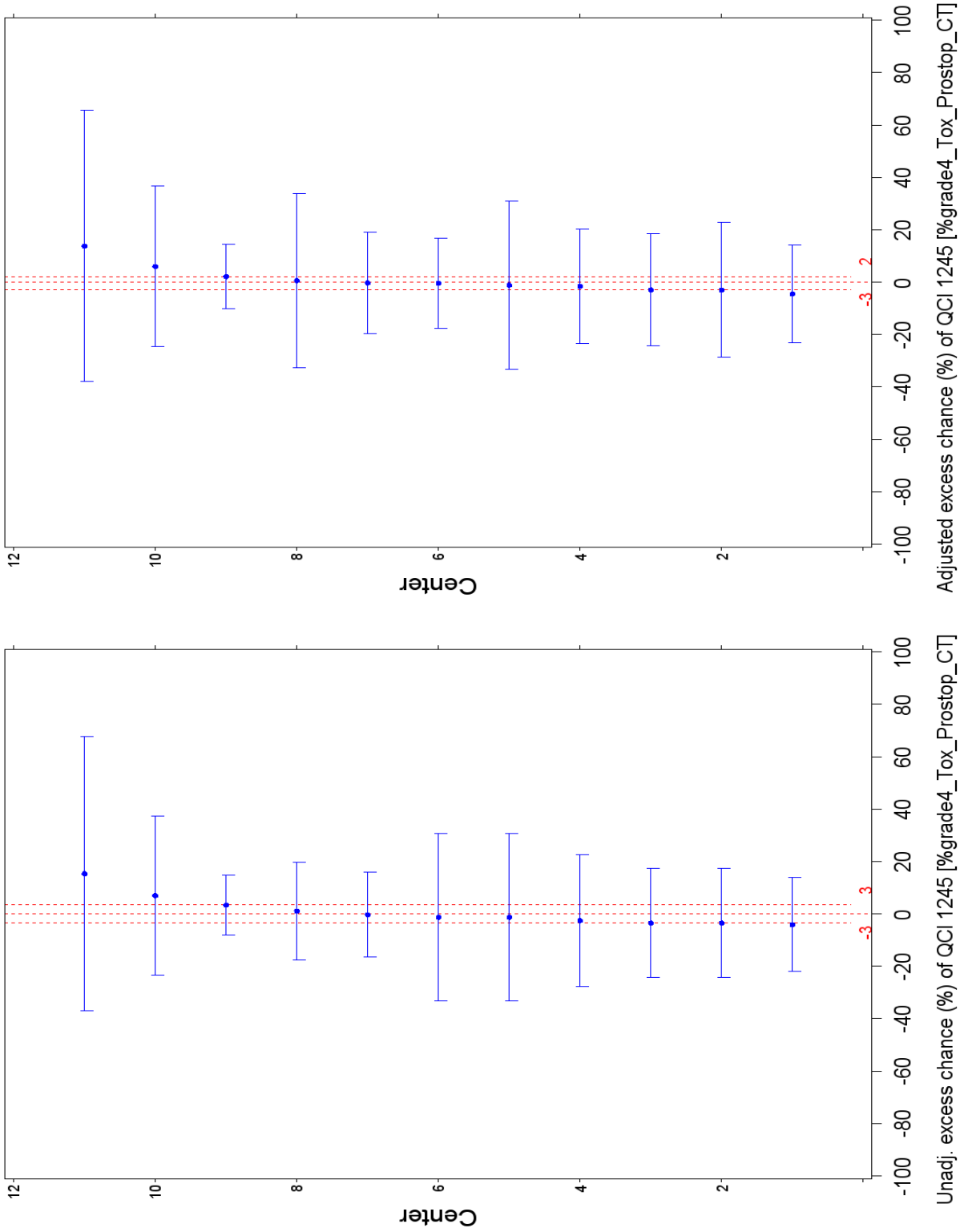


Figure 48: QCI 1245 [%grade4_Tox_Prostop_CT] (outcome): Rate of acute grade 4 chemotherapy-related complications
Above: Adj. excess probability (%), relative to the average center.
Below: Unadj. excess probability (%), relative to the average center.

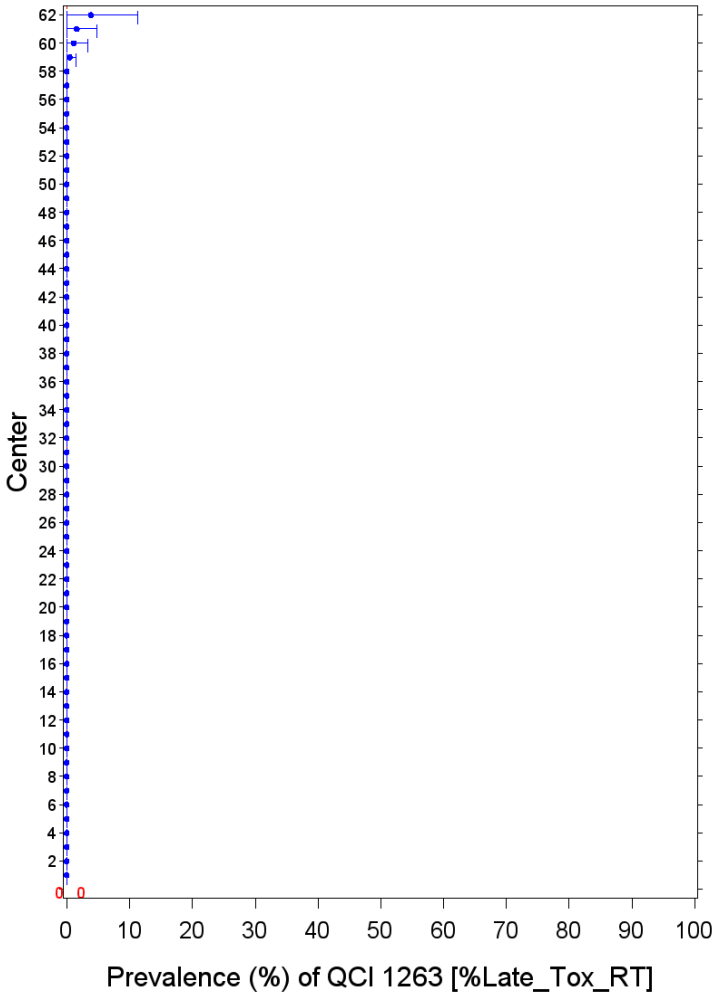


1.7 QUALITY INDICATORS RELATED TO FOLLOW-UP

Table 52: QCI 1263 [%Late_Tox_RT] (outcome): Late grade 4 complications of radiotherapy or chemoradiation Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (1428)	1890 (57%)	4 (0%)
[1-10[	68 (23)	45 (66%)	0 (0%)
[10-20[	218 (108)	110 (50%)	0 (0%)
[20-40[	422 (195)	227 (54%)	1 (0%)
[40-60[	663 (316)	347 (52%)	0 (0%)
[60-80[	399 (198)	201 (50%)	0 (0%)
[80-100[	523 (269)	254 (49%)	0 (0%)
[100-]	1025 (319)	706 (69%)	3 (0%)

Figure 49: QCI 1263 [%Late_Tox_RT] (outcome): Late grade 4 complications of radiotherapy or chemoradiation, prevalence (%) among eligible cases.



1.8 QUALITY INDICATORS RELATED TO HISTOPATHOLOGIC EXAMINATION

Table 53: QCI 1271 [%Path_Rep_Use] (process): Use of the pathology report sheet.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (452)	1980 (60%)	1938 (98%)
[1-10[	68 (10)	26 (38%)	25 (96%)
[10-20[	218 (44)	100 (46%)	100 (100%)
[20-40[	422 (51)	267 (63%)	264 (99%)
[40-60[	663 (81)	390 (59%)	374 (96%)
[60-80[	399 (68)	226 (57%)	225 (100%)
[80-100[	523 (108)	300 (57%)	286 (95%)
[100-]	1025 (90)	671 (65%)	664 (99%)

Figure 50: QCI 1271 [%Path_Rep_Use] (process): Use of the pathology report sheet.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

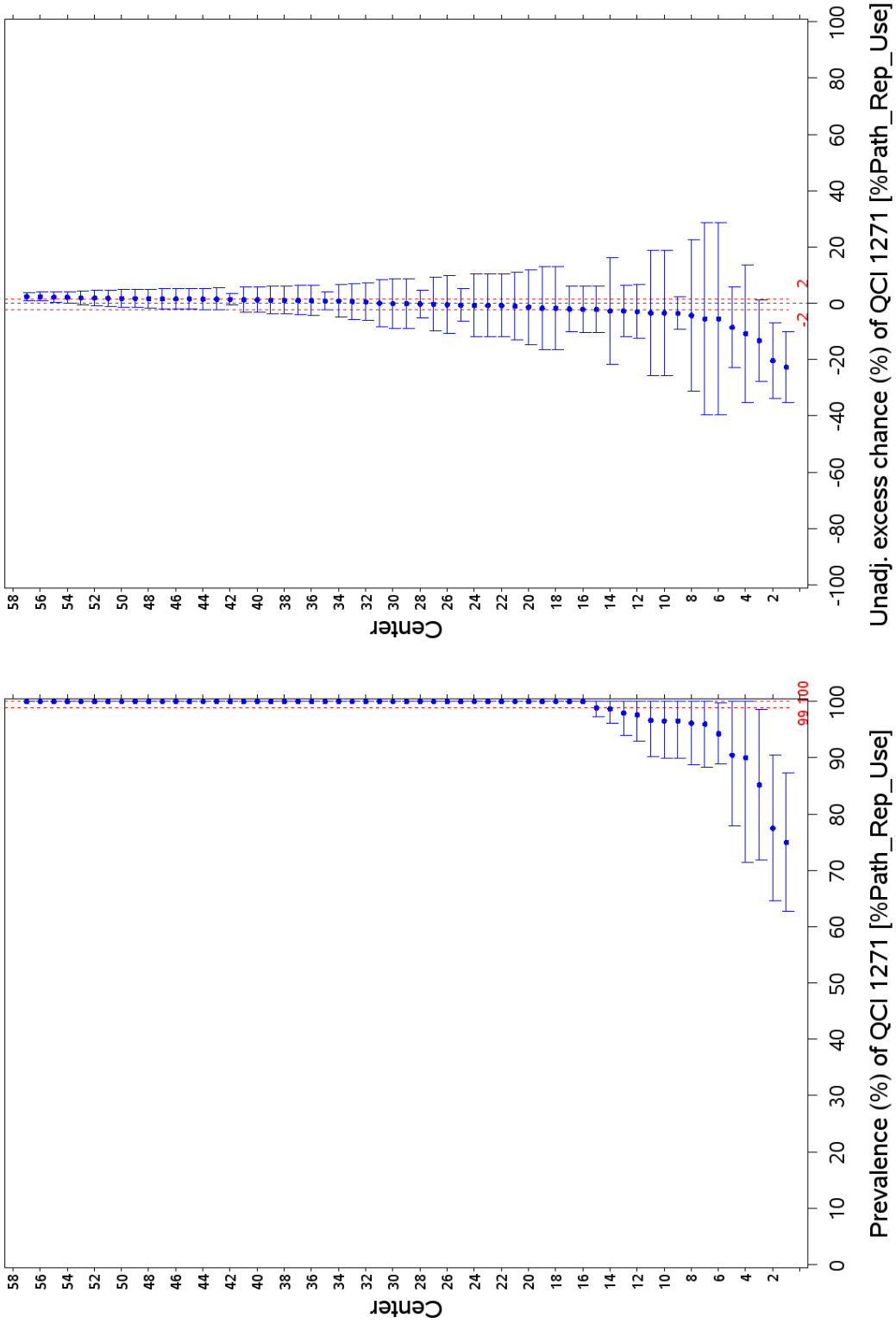


Table 54: QCI 1272 [%TME_Qual_Rep] (process): Quality of TME assessed according to Quirke and mentioned in the pathology report.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (486)	1572 (47%)	1074 (68%)
[1-10[	68 (10)	26 (38%)	19 (73%)
[10-20[	218 (45)	71 (33%)	47 (66%)
[20-40[	422 (63)	196 (46%)	123 (63%)
[40-60[	663 (89)	262 (40%)	155 (59%)
[60-80[	399 (69)	203 (51%)	136 (67%)
[80-100[	523 (109)	249 (48%)	149 (60%)
[100-]	1025 (101)	565 (55%)	445 (79%)

Figure 51: QCI 1272 [%TME_Qual_Rep] (process): Quality of TME assessed according to Quirke and mentioned in the pathology report.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

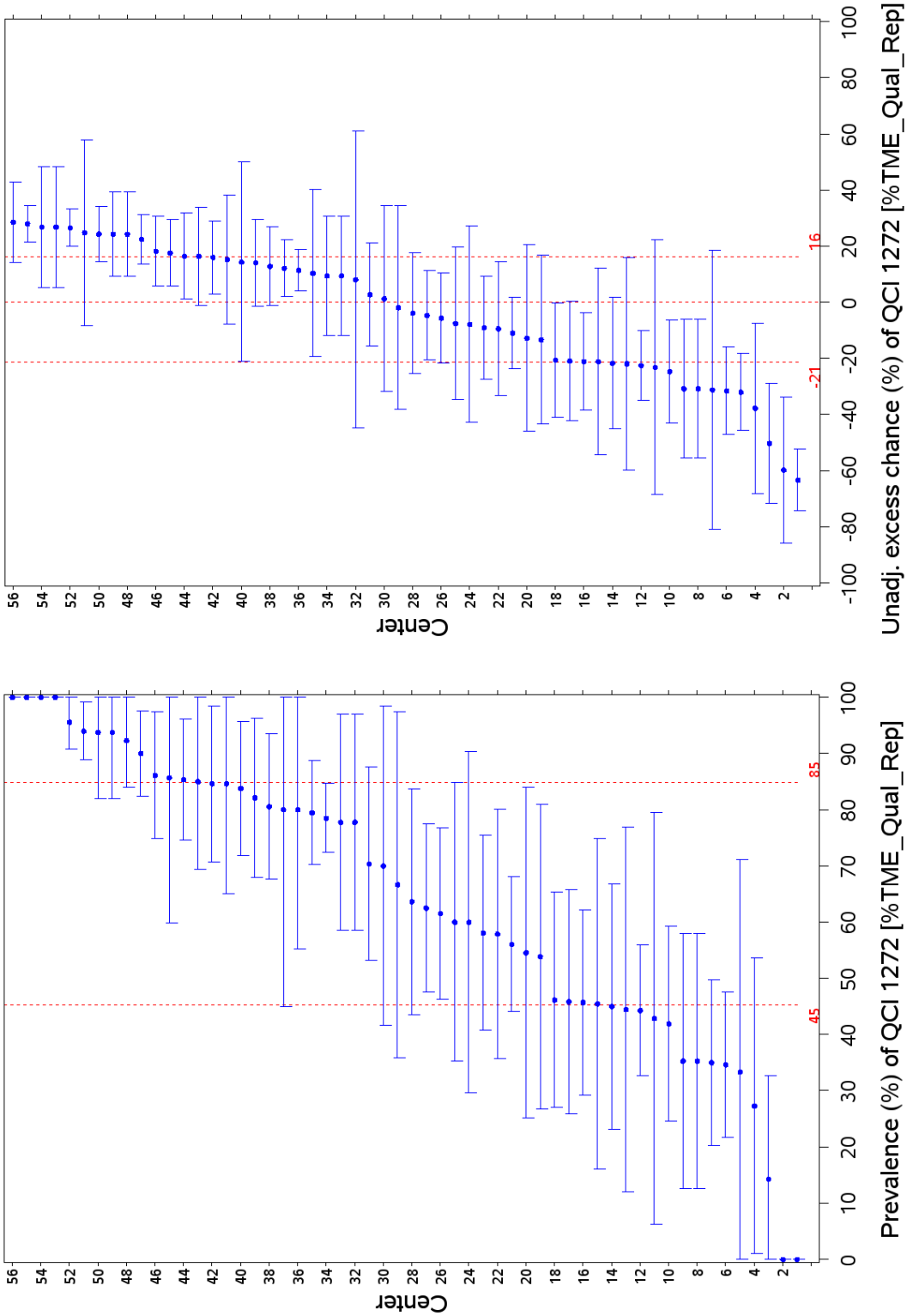


**Table 55: QCI 1273 [%Dist_Margin_Rep] (process): Distal tumor-free margin mentioned in the pathology report.
Missingness, eligibility and prevalence information.**

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (385)	2051 (62%)	1763 (86%)
[1-10[	68 (9)	39 (57%)	35 (90%)
[10-20[	218 (40)	130 (60%)	89 (68%)
[20-40[	422 (42)	253 (60%)	224 (89%)
[40-60[	663 (69)	415 (63%)	350 (84%)
[60-80[	399 (61)	243 (61%)	213 (88%)
[80-100[	523 (93)	312 (60%)	267 (86%)
[100-]	1025 (71)	659 (64%)	585 (89%)

Figure 52: QCI 1273 [%Dist_Margin_Rep] (process): Distal tumor-free margin mentioned in the pathology report.

Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

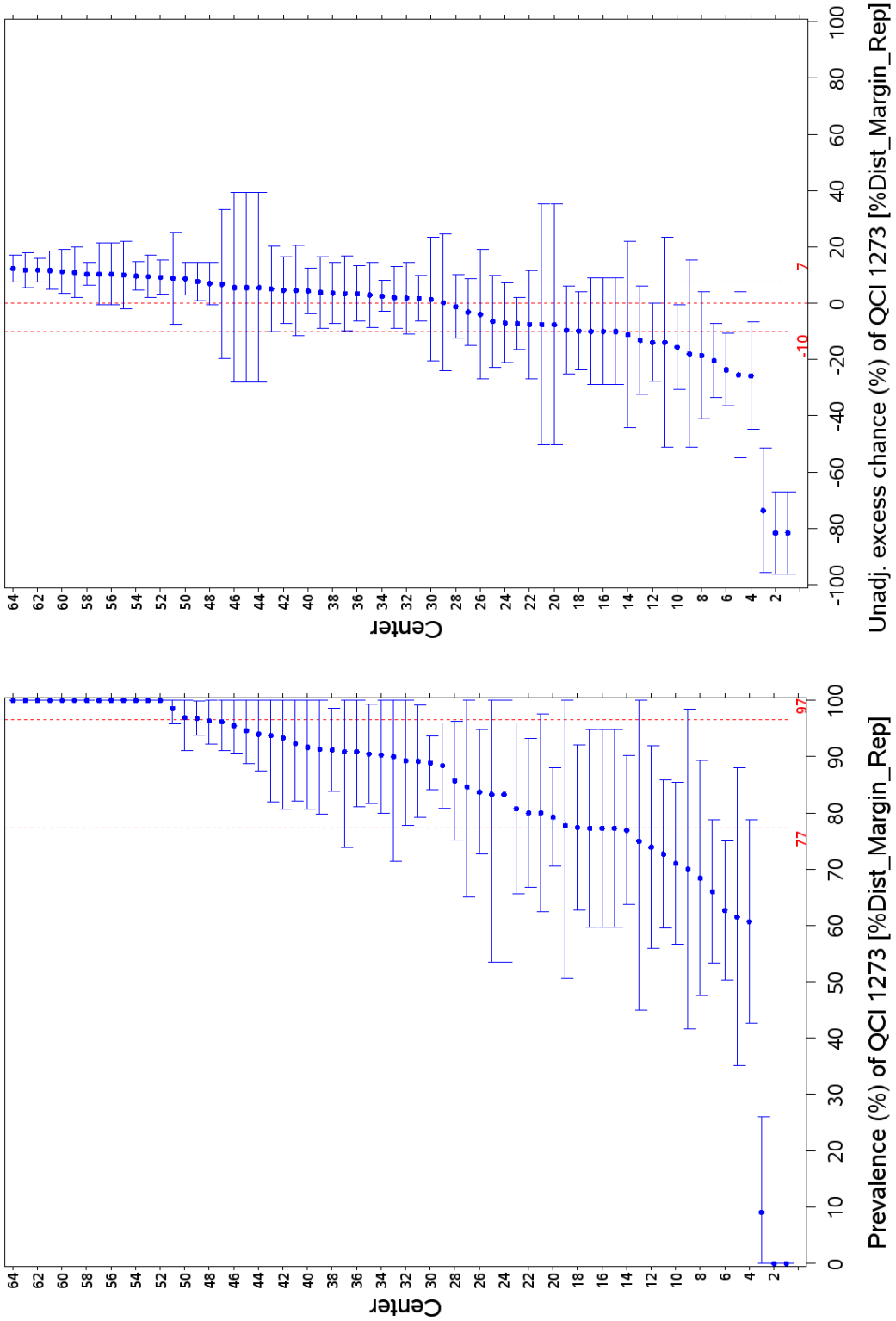


Table 56: QCI 1273b [%Dist_Margin_Pos_Rep] (process): Distal margin involvement mentioned after SSO or Hartmann.

Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (428)	2034 (61%)	1860 (91%)
[1-10[	68 (10)	38 (56%)	36 (95%)
[10-20[	218 (40)	131 (60%)	96 (73%)
[20-40[	422 (45)	253 (60%)	229 (91%)
[40-60[	663 (85)	403 (61%)	368 (91%)
[60-80[	399 (62)	242 (61%)	232 (96%)
[80-100[	523 (108)	304 (58%)	265 (87%)
[100-]	1025 (78)	663 (65%)	634 (96%)

Figure 53: QCI 1273b [%Dist_Margin_Pos_Rep] (process): Distal margin involvement mentioned after SSO or Hartmann.

Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

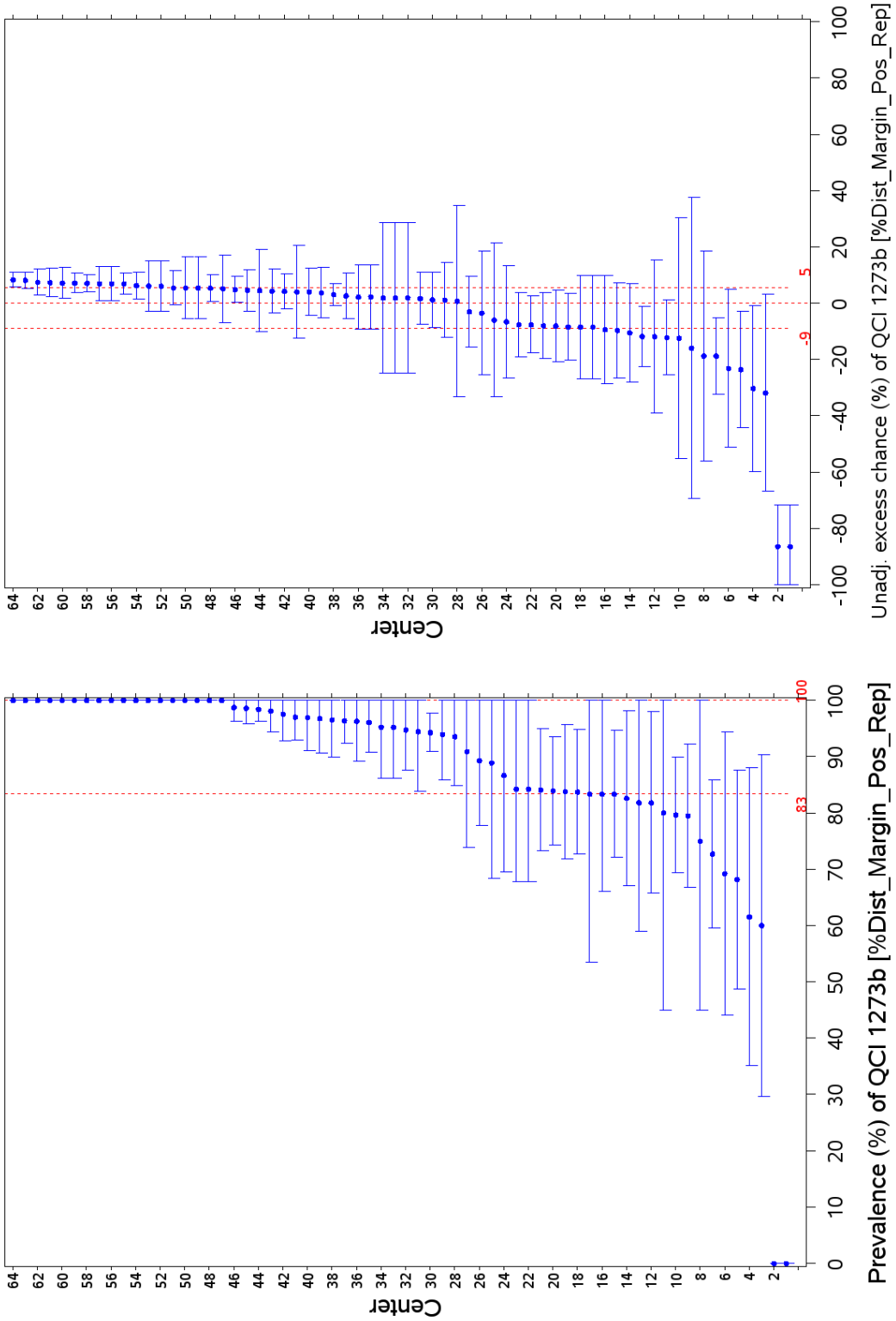


Table 57: QCI 1274 [#Nodes_examined] (process): Number of lymph nodes examined.

Statistical summary of the distribution of this QCI.

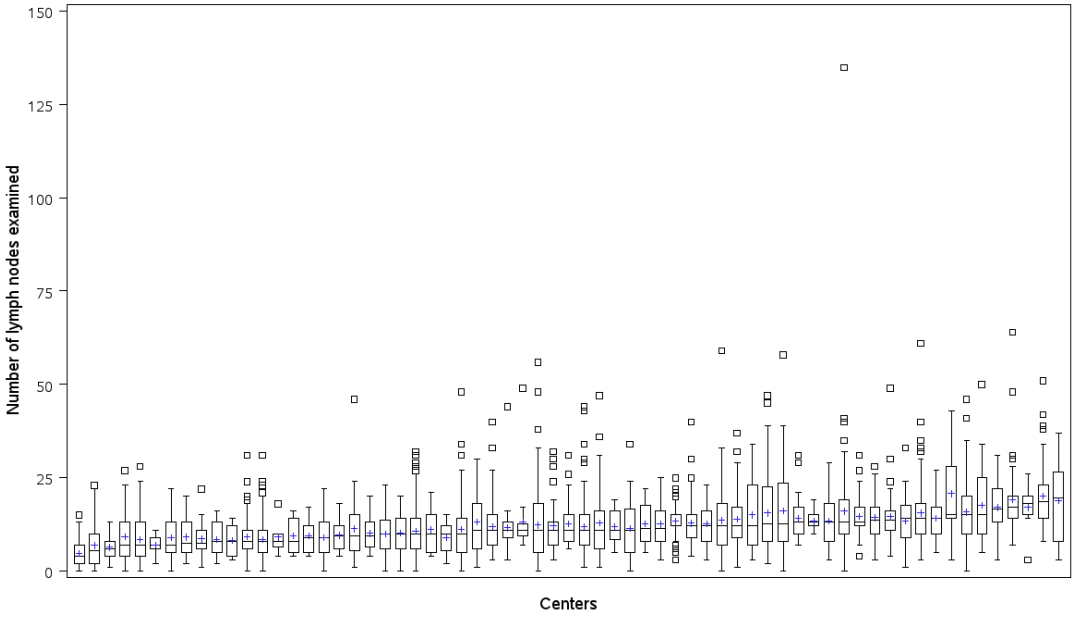
Center	Total N (missing)	N (%) eligible	Min	P25	P50	P75	Max
TOTAL	3318 (594)	2714 (82%)	0	7	11	16	135
[1-10[	68 (10)	58 (85%)	2	6	10	14	22
[10-20[	218 (75)	142 (65%)	0	6	11	15	43
[20-40[	422 (76)	346 (82%)	0	7	11	15	50
[40-60[	663 (121)	539 (81%)	0	7	11	16	58
[60-80[	399 (65)	334 (84%)	0	10	14	19	64
[80-100[	523 (151)	372 (71%)	1	9	13	17	61
[100-]	1025 (96)	923 (90%)	0	6	10	14	135

Table 58: Truncated QCI 1274 [#Nodes_examined] (process): Number of lymph nodes examined, truncated at 25 nodes.

Statistical summary of the distribution of this truncated QCI.

Center	Total N (missing)	N (%) eligible	Min	P25	P50	P75	Max
TOTAL	3318 (594)	2714 (82%)	0	7	11	16	25
[1-10[	68 (10)	58 (85%)	2	6	10	14	22
[10-20[	218 (75)	142 (65%)	0	6	11	15	25
[20-40[	422 (76)	346 (82%)	0	7	11	15	25
[40-60[	663 (121)	539 (81%)	0	7	11	16	25
[60-80[	399 (65)	334 (84%)	0	10	14	19	25
[80-100[	523 (151)	372 (71%)	1	9	13	17	25
[100-]	1025 (96)	923 (90%)	0	6	10	14	25

Figure 54: Box plots of QCI 1274 [#Nodes_Examined] in individual centers, sorted by median number of lymph nodes examined ('-' = median; '+' = mean; '□' = outlying observation).
Above: Original values.
Below: Values truncated at 25 nodes.



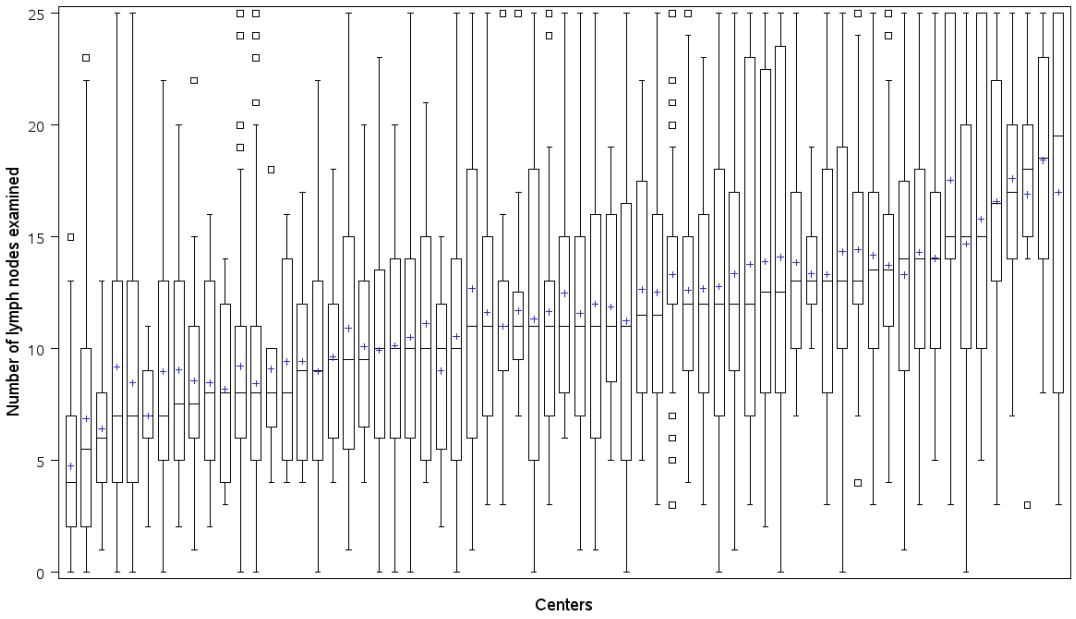


Figure 55: QCI 1274 [#Nodes_Examined] (process): Number of lymph nodes examined.
Unadjusted excess (truncated).number of nodes examined, relative to the average center.

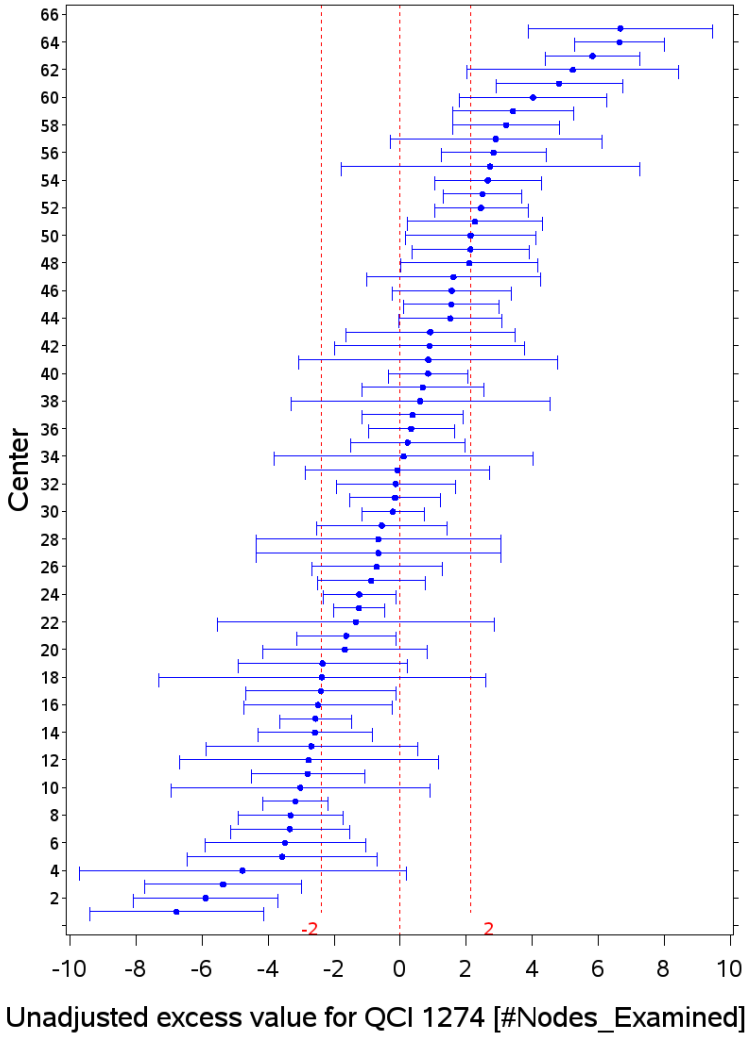


Table 59: QCI 1275 [%CRM_mm_Rep] (process): Mesorectal (y)pCRM mentioned in the pathology report if radical surgical resection.
Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (292)	2615 (79%)	1932 (74%)
[1-10[	68 (7)	55 (81%)	43 (78%)
[10-20[	218 (27)	172 (79%)	90 (52%)
[20-40[	422 (24)	355 (84%)	254 (72%)
[40-60[	663 (61)	529 (80%)	366 (69%)
[60-80[	399 (50)	322 (81%)	247 (77%)
[80-100[	523 (73)	368 (70%)	290 (79%)
[100-]	1025 (50)	814 (79%)	642 (79%)

Figure 56: QCI 1275 [%CRM_mm_Rep] (process): Mesorectal (y)pCRM mentioned in the pathology report if radical surgical resection.
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.

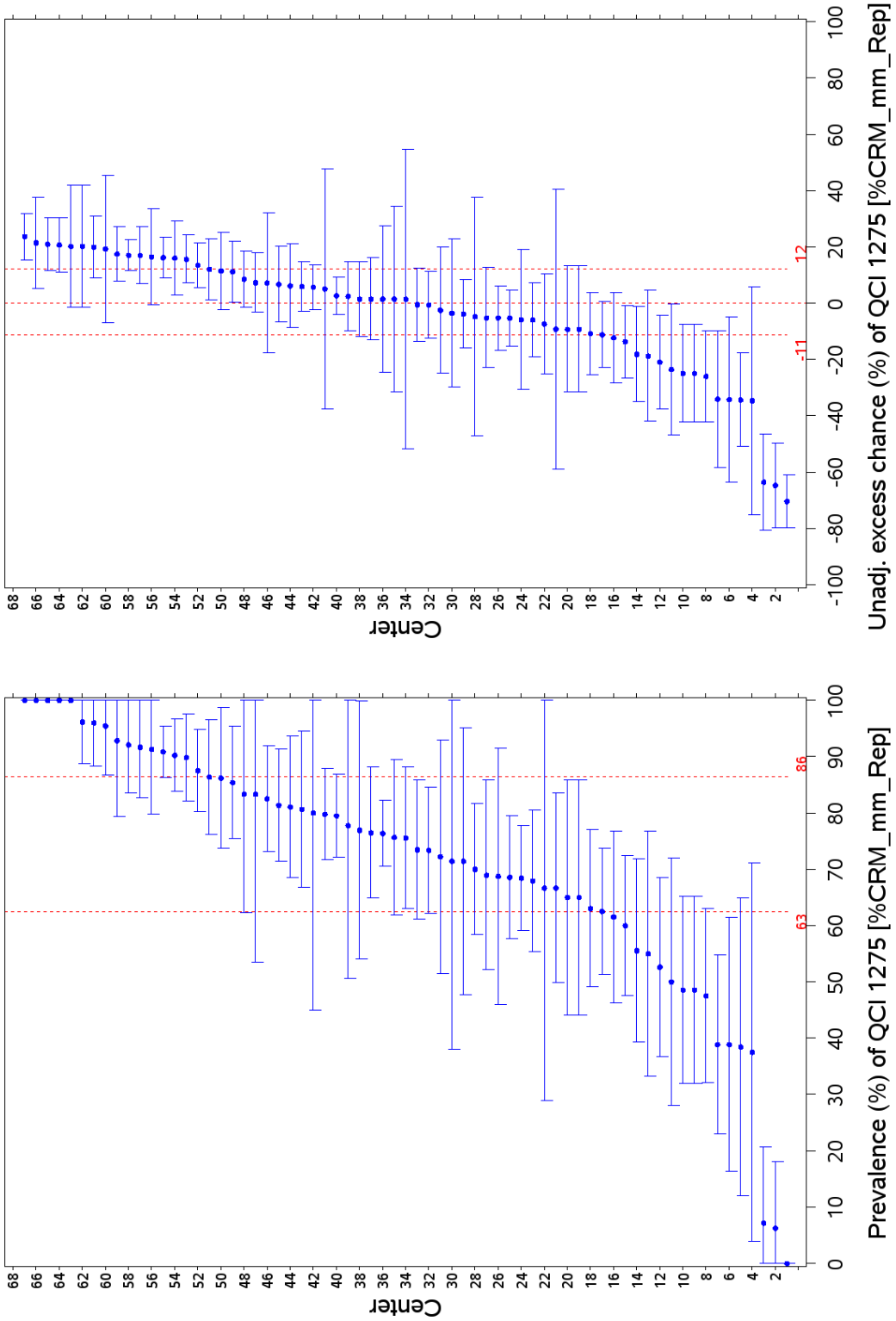
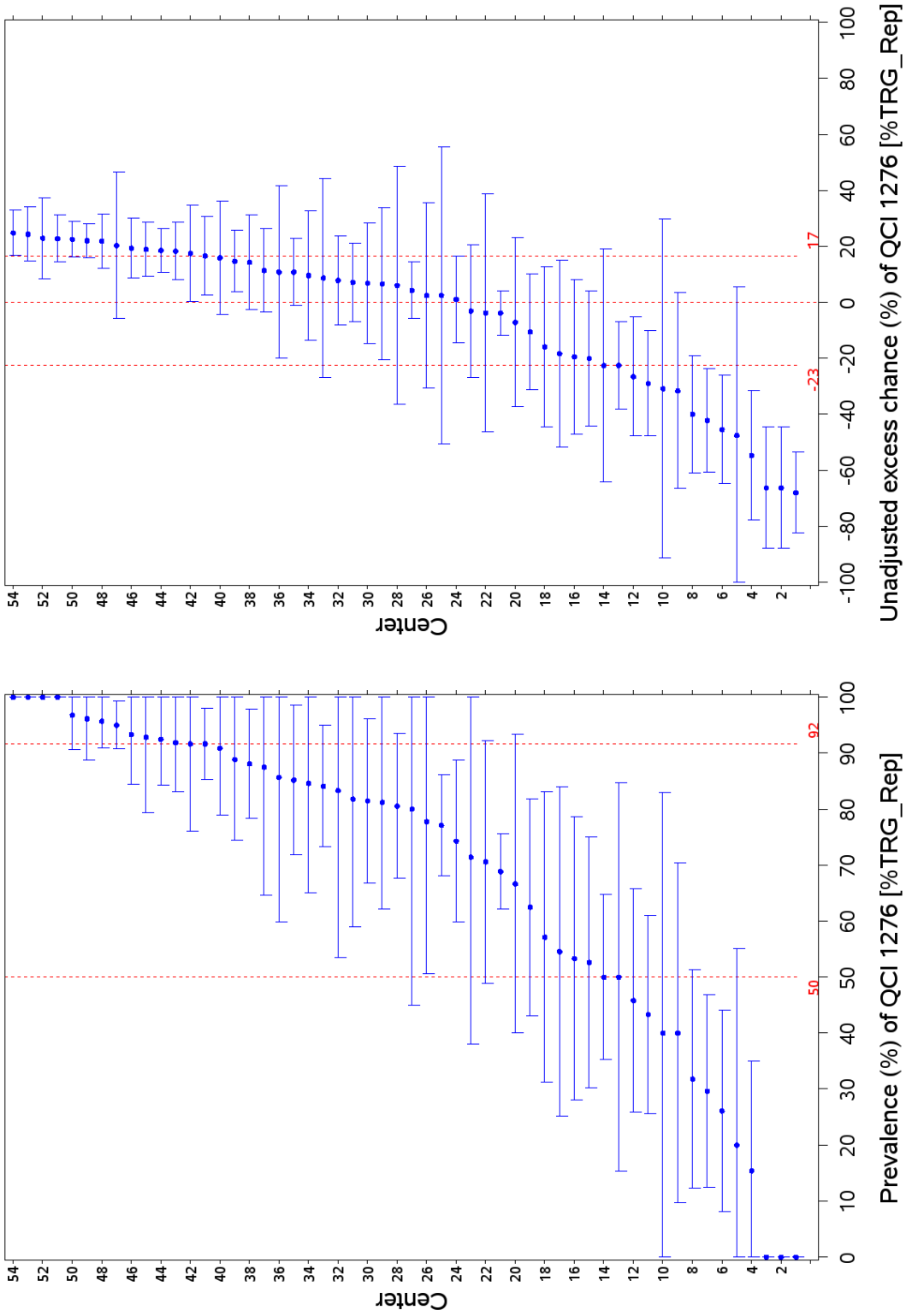


Table 60: QCI 1276 [%TRG_Rep] (process): Tumor regression grade (Dworak) mentioned in the pathology report (after long course neoadjuvant treatment).

Missingness, eligibility and prevalence information.

Center	Total N (missing)	N (%) eligible	N (%) events
TOTAL	3318 (500)	1427 (43%)	1069 (75%)
[1-10[	68 (14)	33 (49%)	17 (52%)
[10-20[	218 (44)	83 (38%)	44 (53%)
[20-40[	422 (62)	186 (44%)	123 (66%)
[40-60[	663 (104)	240 (36%)	161 (67%)
[60-80[	399 (65)	139 (35%)	122 (88%)
[80-100[	523 (101)	202 (39%)	157 (78%)
[100-]	1025 (110)	544 (53%)	445 (82%)

Figure 57: QCI 1276 [%TRG_Rep] (process): Tumor regression grade (Dworak) mentioned in the pathology report (after long course neoadjuvant treatment).
Above: Unadj. excess probability (%), relative to the average center.
Below: Prevalence (%) among eligible cases.



2 QUALITY OF CARE INDICATORS

We follow the list of QCIs as presented in the PROCARE consensus of July 24th, 2010, summarized in Appendix 4. Sections on outcome indicators are marked with a '*' in the beginning of their title.

Note that for the statistical analyses per QCI, the 10 patients with cStage 0 will be discarded from the database, leaving a total of 3318 patients in the database.

2.1 GENERAL QUALITY INDICATORS

The definitions as provided in the PROCARE documents are clear in principle, but for good practice these QCIs need to be translated into technically correct working definitions containing the observed time and endpoint, which may be either the event of interest, a competing event or censoring.

Censoring happens for patients for whom no event of interest was observed before closure of the database. The current PROCARE database was closed at the end of October 2010 and was linked with the death records of the version of the Cross Banks Social Security database of August 2010. The BCR argues that we may then be confident that all deaths up to July 31st, 2010 are registered in the database we have at our disposal. Therefore, July 31st, 2010 will be used as the administrative censoring date for the current PROCARE database.

2.1.1 QCI 1111 [OS]

This QCI has been explained in more detail in the main report (section 3.4.1).

2.1.2 *Disease-specific 5-year survival by stage (QCI 1112, outcome)

2.1.2.1 Definition

PROCARE definition

N: Number of patients in denominator that did not die from rectal cancer during 1-5 years follow-up.

D: Number of patients for whom the national registry number is known and have a follow-up of 1 -5 years, respectively. Survival status was obtained through cross-link with the Crossroads Bank for Social Security (CBSS).

Patients who died without rectal cancer (local recurrence or metastasis) are censored. Survival curves were calculated using the Kaplan Meier method.

Working definition

Cumulative incidence based probability of not dying from rectal cancer within 5 years after rectum cancer diagnosis. This involves follow-up time (in years) and as event the endpoint 'death from rectal cancer' (defined as 'with record of local recurrence or distant metastasis'). The other types of endpoints here are either censoring (subsequent risk of disease-specific death is unaltered but masked from view) and 'death from other causes' which is a competing risk (subsequent risk of disease-specific death = 0).

D: Number of patients for whom the national registry number is known and for whom the incidence date is known to be before the administrative censoring date. Additionally, deceased patients according to the CBSS, but for whom no follow-up information is available in the PROCARE database are excluded from the denominator.

Note that 5-year survival probabilities will for now be replaced with 3-year survival probabilities.

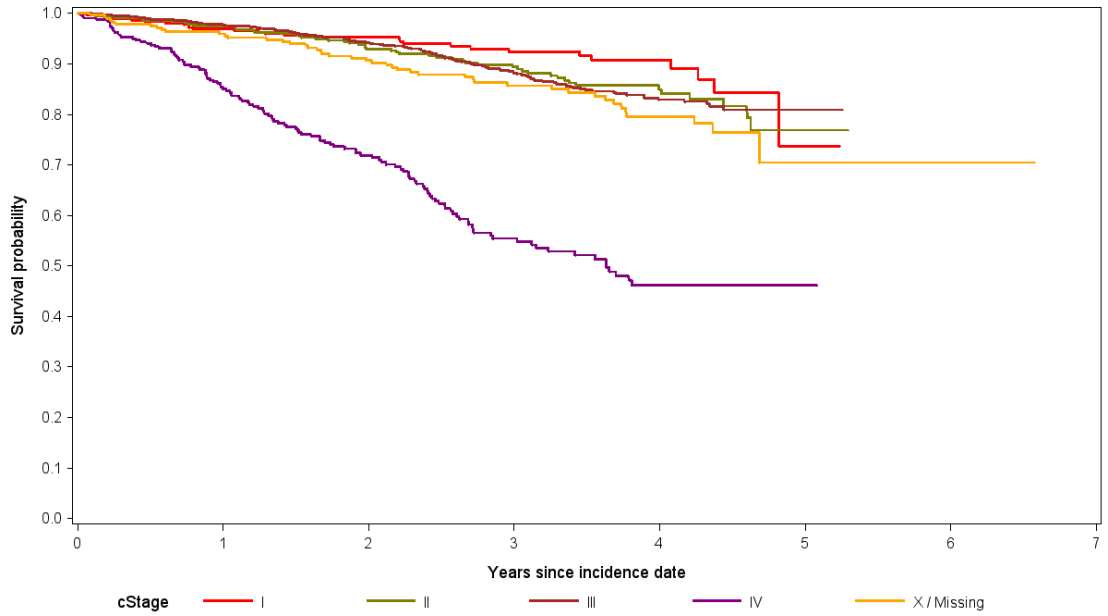
Note that due to the low quality of the follow-up information in the PROCARE database the general quality of this QCI is questionable.

2.1.2.2 Description

A total of 2807 of the 3318 (85%) patients meet the requirements for the denominator of this QCI. Of the 511 patients who are not eligible. 507 have missing information (on social security number, incidence date, follow-up in case of death) and the other 4 have an incidence date after July 31st, 2010.

Of the 2807 eligible patients, 193 (7%) patients died with local recurrence and/or distant metastasis and 210 (7%) patients died without (reported) local recurrence nor distant metastasis. After merging centers with less than 5 eligible patients into one overlapping center, 67 centers remain for performance evaluation in terms of disease-specific survival. More detail per size-grouped centers on the follow-up time, person years and event rate can be found in Table 16 in Section 1. The cStage-stratified survival (i.e. 1 - cumulative incidence) curves are presented in Figure 58, the corresponding (y)pStage-stratified survival curves are presented in Figure 6 of Section 1. The graphs show the probability of surviving rectal cancer or dying without local recurrence nor distant metastasis, accounting for the fact that indeed some patients die of other causes.

Figure 58: cStage-stratified cumulative incidence-based survival curves for QCI 1112 [DSS], estimating the (unadjusted) probability of surviving rectal cancer or dying without local recurrence nor distant metastasis by t years after the incidence of rectum cancer.



2.1.2.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

Appendix 2 contains a list of prognostic factors for cancer-specific survival. We restrict ourselves to pre-treatment prognostic factors of which BMI, age and TNM-stage are available in the PROCARE database.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the following factors are suggested to be used for adjustment: age > 70 years, gender, extraperitoneal location, (y)pN+, no tumor response to long course radio(chemo)therapy.

Of these, the former 3 will be considered when building the risk-adjustment model for this QCI. The latter 2 however are post-treatment factors, which can already be influenced by the quality of care provided by a certain center, and would hence 'cover' part of the center effect. Note that the (clinical) nodal status is partly considered through stratification by cStage.

Empirical associations

Significant univariate associations between the available prognostic factors and cStage-stratified survival for the event of interest (death with local recurrence or distant metastasis) are presented in Table 61. The interpretation of the hazard ratios is explained in the main report (section 3.4.2.1, Tables 25 and 26).

Table 61: Hazard ratio [95% Wald confidence interval] estimate and corresponding p-value from univariate cStage-stratified Cox regression models for QCI 1112 [DSS]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Hazard ratio [95% CI]	*p*-value
Age	(continuous)	1.03 [1.02, 1.05]	< 0.0001
ASA score [ref. = I]	II	1.34 [0.89, 2.00]	< 0.0001
	III-V	2.59 [1.67, 4.02]	
	Missing	1.99 [1.24, 3.19]	
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	3.13 [1.53, 6.41]	0.007
	Missing	0.99 [0.55, 1.79]	
cT4 [ref. = No]	Yes	1.70 [1.17, 2.46]	0.006
	Missing	0.64 [0.32, 1.28]	
Preoper. incontinence [ref. = No]	Yes	1.53 [1.05, 2.21]	0.05
	Missing	0.57 [0.18, 1.80]	

2.1.2.4 Estimation of unadjusted and case mix adjusted center effects

Because there are two possible events (the event of interest and a competing event) for this QCI, center-effects should be obtained from a competing risks analysis instead of a standard survival analysis.

A model building procedure was performed to identify joint associations between prognostic factors and disease-specific survival, stratified by cStage. For this, we consider two cause-specific survival models, one for the event of interest (death with local recurrence or distant metastasis) and one for the competing event (death without local recurrence and distant metastasis). In this, the prognostic factors gender, age, BMI, ASA co-morbidity score and level of the tumor (high, mid or low) were considered.

For the event of interest, this yields a model with main effects for gender, ASA score and age (with a different slope before and after the breakpoint of 70 years), with the competing event BMI and its missingness indicator additionally retained in the final model. There are no significant interactions between the prognostic factors in both models. The hazard ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 62.

Table 62: Hazard ratio [95% Wald confidence interval] estimate and corresponding p-value from the final multivariate cStage-stratified Cox regression model for QCI 1112 [DSS], both for the event of interest and the competing event. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Event of interest			Competing event		
		Hazard ratio [95% CI]	*p*-value	Joint *p*-value	Hazard ratio [95% CI]	*p*-value	Joint *p*-value
Age	(cont.)	1.00 [0.98, 1.02]	0.80	< 0.0001	1.01 [0.98, 1.03]	0.58	< 0.0001
Age (+ 70 years)	(cont.)	1.08 [1.04, 1.13]	0.0006		1.09 [1.04, 1.14]	0.0003	
Gender [ref. = Male]	Female	0.92 [0.68, 1.25]	0.60		0.71 [0.52, 0.96]	0.03	
ASA score [ref. = I]	II	1.01 [0.64, 1.60]	0.01		1.18 [0.70, 1.99]	< 0.0001	
	III-V	1.67 [0.98, 2.85]			3.80 [2.19, 6.60]		
	Missing	1.91 [1.08, 3.36]			2.44 [1.34, 4.46]		
BMI	(cont.)				1.00 [0.96, 1.04]	0.98	0.02
Missing BMI [ref. = Not missing]	Missing				1.72 [0.59, 5.00]	0.32	

Adjusted center effects are estimated from a competing risk analysis, starting from two cause-specific Firth-corrected Cox regression models (one for the event of interest and one for the competing event). Center effects are expressed as the 'excess' probability of avoiding death with local recurrence or distant metastasis for 3 years. relative to the 'average' center.

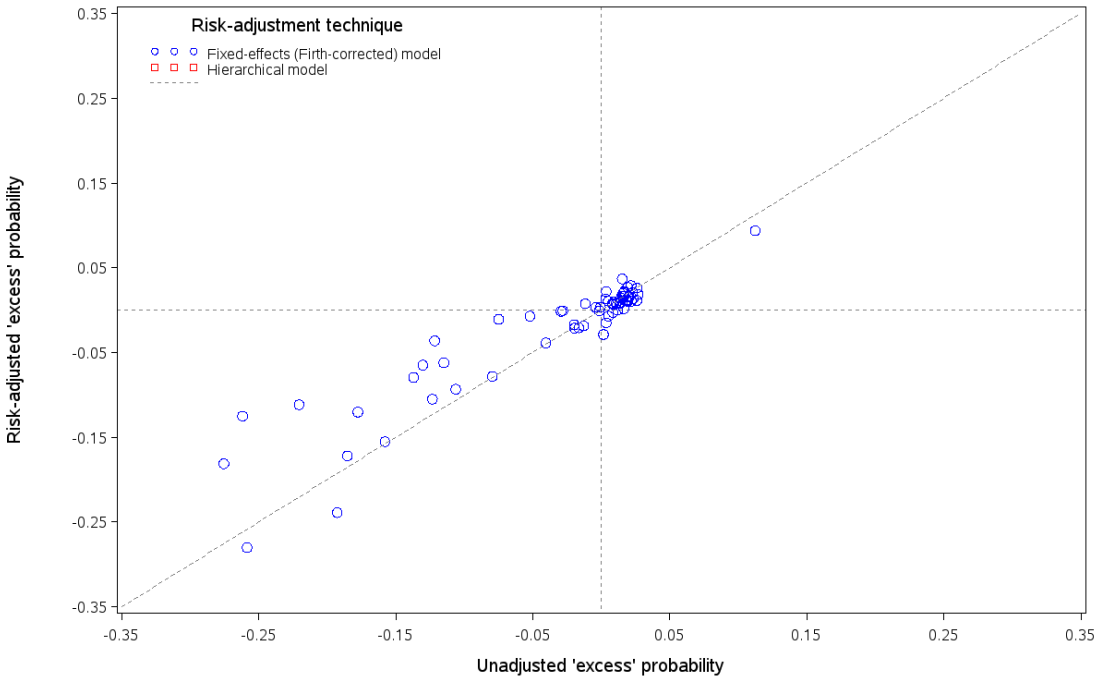
A basic summary of the distribution of center effects as estimated from the unadjusted analysis and the fixed-effects adjusted analyses is presented in Table 63.

Table 63: Minimum, P25, P75, maximum and interquartile range of the center-effects (%) for QCI 1112 [DSS] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-28	-5	2	11	7
Fixed-effects regression	-28	-3	2	9	5

Figure 59 shows the relation between adjusted and unadjusted center effects. From this we learn the center effects obtained from the fixed-effects adjustment model stay generally close to the unadjusted center effects

Figure 59: Scatter plot of adjusted center effects (from fixed-effects outcome regression) versus unadjusted center effects for QCI 1112 [DSS].



2.1.3 *Relative survival (new QCI 1112b, outcome)

2.1.3.1 Definition

The relative survival is the ratio of observed survival in a diseased population to the expected survival rate in the corresponding general population. It estimates the relative chance that a patient will survive a set number of years after a cancer diagnosis. It is calculated to exclude the chance of death from diseases other than the cancer and points to whether or not that specific disease shortens a person's life.

If reliable information on cause of death is available, it is preferable to use the 'adjusted rate', i.e. disease (rectal cancer)-specific survival obtained on the observed data. This is particularly true when the series is small or when the patients are largely drawn from a particular segment of the population (e.g. socioeconomic segment).

2.1.3.2 Description

As this QCI was added to the QCI list by PROCARE after the start of this project and it requires a somewhat different analysis technique than the other survival-related QCIs, it is not further considered in this report.

2.1.4 *Proportion of patients with local recurrence (QCI 1113, outcome)

2.1.4.1 Definition

PROCARE definition

N: Number of patients in denominator who developed a local recurrence at 1-5 year.

D: Number of (y)pStage 0-III patients with R0 resection who have a follow-up of 1-5 years, respectively.

Working definition

Cumulative incidence based probability of surviving 5-years without local recurrence for patients in the denominator. This involves follow-up time (in years) and as event the endpoint 'local recurrence' or censoring. Death without local recurrence is considered a competing risk.

D: Number of (y)pStage 0-III patients with R0 resection for whom the national registry number is known, the incidence date is known to be before the administrative censoring date, there has been at least one follow-up report filed and the date of local recurrence is known or can be reconstructed based on other information.

Note that given the poor quality of the follow-up data, this QCI mainly provides information on whether a certain center provides follow-up information or not.

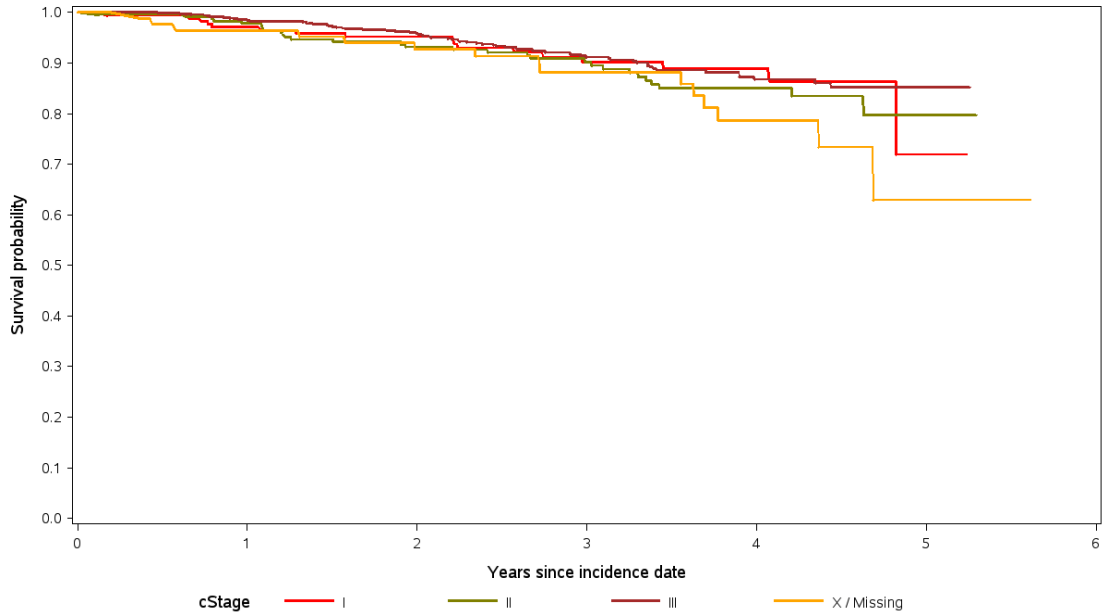
Note that this QCI is not stratified by a staging variable (except in Figure 60).

2.1.4.2 Description

Together 1186 of the 3318 (36%) patients meet the requirements for the denominator of this QCI. Of the 2132 patients in the PROCARE database who are not eligible, for 1776 this is because of missing information and the other 356 have either an incidence date after July 31st, 2010, (y)pStage IV or not an R0 resection.

Of the 1186 eligible patients, 29 (2%) patients had a local recurrence and 98 (8%) patients died without a (reported) local recurrence. After merging centers with less than 5 eligible patients into one overlapping center, 50 centers remain to evaluate performance in terms of local recurrence survival. More detail per size-grouped center on the follow-up time, person years and event rate can be found in Table 17 in Section 1. The cStage-stratified survival (i.e. 1 - cumulative incidence) curves are presented in Figure 60, the corresponding (y)pStage-stratified survival curves are presented in Figure 7 of Section 1. The graphs show the probability of avoiding a local recurrence until time t (which may include death without local recurrence by time t).

Figure 60: cStage-stratified cumulative incidence-based survival curves for QCI 1113 [LRFS], estimating the probability (unadjusted) of avoiding a local recurrence up until t years after the incidence of rectum cancer (possibly because of death without recurrence before year t).



2.1.4.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

Appendix 2 contains an list of prognostic factors for cancer-specific survival. Given our findings in Section 1, we restrict ourselves to pre-treatment prognostic factors of which tumor level, T-stage, N-stage and gender are available in the PROCARE database.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the following factors are suggested to be used for adjustment: tumor level (<5cm) , (y)pT (3/4), (y)pN, (y)pSt II/III, no downstaging, venous involvement.

Of these, the former 4 will be considered when building the risk-adjustment model for this QCI, after switching the (y)pT4 to cT4, (y)pN to cN and (y)pSt II/III to cSt II/III. Downstaging will not be considered since this involves a post-treatment factor, which can already be influenced by the quality of care provided by a certain center. Venous involvement was not found in the database.

Empirical associations

Of the considered prognostic factors, only tumor location (ventral versus not or missing) is significantly associated with the intensity of local recurrences, see Table 64. The interpretation of the hazard ratios is as explained in the main report (section 3.4.1)

Table 64: Hazard ratio [95% Wald confidence interval] estimate and corresponding p-value from univariate Cox regression models for QCI 1113 [LRFS]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Hazard ratio [95% CI]	*p*-value
Ventral tumor [ref. = No]	Yes	0.33 [0.11, 0.95]	0.05
	Missing	0.32 [0.08, 1.37]	

2.1.4.4 Estimation of unadjusted and case mix adjusted center effects

Because there are very few (2%) events of interest (local recurrence) it was not possible to fit a stable proportional hazards model with an indicator variable for each center, hence no unadjusted center effects could be estimated and no model building procedure to identify joint associations between the rate of local recurrence and prognostic factors was performed.

2.1.5 *Disease-free survival (new QCI 1113b, outcome)

2.1.5.1 Definition

PROCARE definition

N: Number of patients in denominator who did not develop a local recurrence and/or distant metastasis at 1-5 year of follow-up.

D: Number of (y)pStage 0-III patients with R0 resection who have a follow-up of 1-5 years, respectively.

Working definition

Kaplan-Meier based probability of 'surviving' 5-years without rectal cancer for patients in the denominator. This involves follow-up time (in years) and as event the first endpoint of death, local recurrence and distant metastasis versus censoring.

D: Number of (y)pStage 0-III patients with R0 resection for whom the national registry number is known, the incidence date is known to be before the administrative censoring date, there has been at least one follow-up report filed and the date of local recurrence or distant metastasis is known or can be reconstructed based on other information.

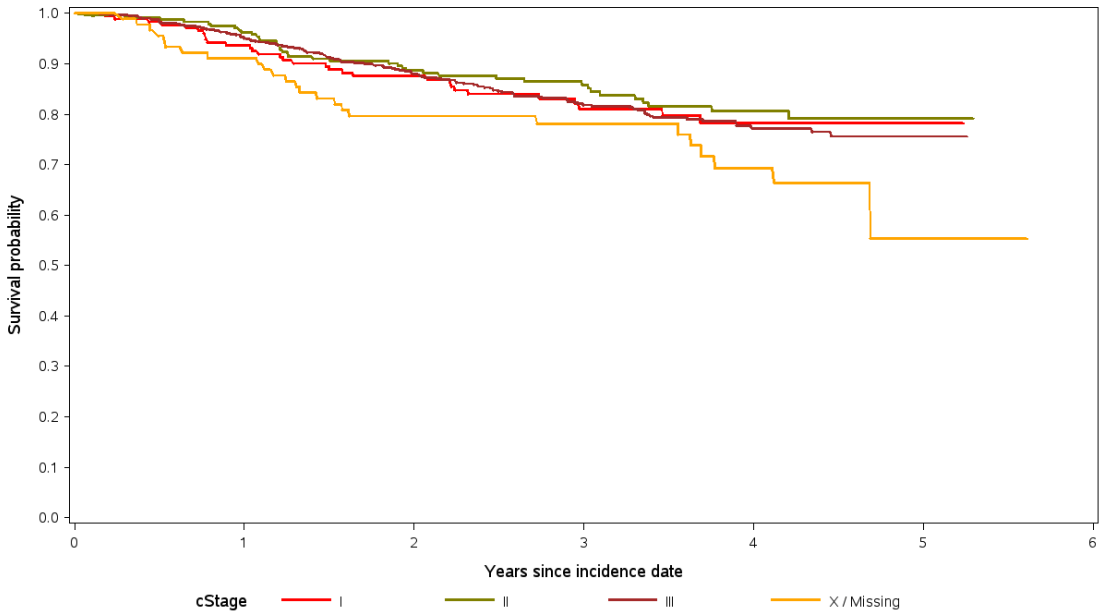
Note that this QCI is not stratified by a staging variable (except for Figure 61).

2.1.5.2 Description

In all, 1234 of the 3318 (37%) patients meet the requirements for the denominator of this QCI. Of the 2084 patients in the PROCARE database who are not eligible, 1680 have missing information and the other 404 have either an incidence date after July 31st, 2010, (y)pStage IV or not an R0 resection.

Of the 1234 eligible patients, 226 (18%) patients had a local recurrence, distant metastasis or died within the observed time period. More detail per size-grouped center on the follow-up time, person years and event rate can be found in Table 18 in Section 1. After merging centers with less than 5 eligible patients into one overlapping center, 50 centers remain to evaluate performance with regard to disease-free survival. The cStage-stratified Kaplan-Meier curves are presented in Figure 61, the corresponding (y)pStage-stratified Kaplan-Meier curves are presented in Figure 8 in Section 1.

Figure 61: Kaplan-Meier curves per cStage stratum, estimating the (unadjusted) probability of surviving and not relapsing t years after the incidence of rectum cancer



2.1.5.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors for disease-free survival were identified.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the following factors are suggested to be used for adjustment: gender, tumor level, cT4, age >70, (y)pT, (y)pN, no tumor response to long course radio(chemo)therapy.

Of these, the former 5 will be considered when building the risk-adjustment model for this QCI, after switching the (y)pT to cT and (y)pN to cN. The latter prognostic factor, however, is no pre-treatment measure and are therefore not eligible for entering our risk-adjustment model.

Empirical associations

Simple associations between available prognostic factors and disease-free survival are presented in Table 65. The interpretation of the hazard ratios is as in the main report section 3.4.1.

Table 65: Hazard ratio [95% Wald confidence interval] estimate and corresponding p-value from univariate Cox regression models for QCI 1113b [DFS]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Hazard ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	1.02 [1.01, 1.03]	0.002	
BMI	(continuous)	1.01 [0.98, 1.04]	0.45	< 0.0001
Missing BMI [ref. = Not missing]	Missing	2.18 [0.92, 5.17]	0.08	
ASA score [ref. = I]	II	1.22 [0.84, 1.75]	0.0001	
	III-V	2.25 [1.52, 3.33]		
	Missing	1.52 [0.91, 2.54]		
Level [ref. = Low]	Mid	1.25 [0.93, 1.68]	0.05	
	High	1.38 [0.96, 2.00]		
	Missing	2.33 [1.17, 4.64]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	3.61 [1.49, 8.77]	0.02	
	Missing	1.26 [0.59, 2.68]		

2.1.5.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects range between -45% and 15% 'excess' probability of no relapse or death 3 years after the incidence of rectal cancer. The P25 and P75 are located at -5% respectively 4%, hence the interquartile range is 9%.

A model building procedure was performed to identify joint associations between prognostic factors and disease-free survival. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cStage, cT4 and level of the tumor (high, mid or low) were considered.

A model with main effects for gender, ASA score, BMI and age (with a different slope before and after the breakpoint of 70 years) was retained. A significant interaction between gender and BMI was found (*p*-value = 0.0836), indicating that survival rates differ for different levels of BMI depending on gender. The hazard ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 66. The interpretation of the hazard ratios in this multivariate model is as in the main report section 3.4.1.

Table 66: Hazard ratio [95% Wald confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) Cox regression model for QCI 1113b [DFS]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Hazard ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	0.99 [0.97, 1.00]	0.12	0.004
Age (+ 70 years)	(continuous)	1.07 [1.03, 1.12]	0.002	
BMI	(continuous)	0.98 [0.94, 1.03]	0.45	0.27
Missing BMI [ref. = Not missing]	Missing	0.86 [0.24, 3.01]	0.81	
Gender [ref. = Male]	Female	0.14 [0.03, 0.85]	0.03	
Gender – BMI interaction [ref. = Male]	(continuous)	1.06 [1.00, 1.14]	0.07	0.08
Gender - Missing BMI interaction [ref. = Male, Not missing]	Female, Missing	7.29 [1.17, 45.38]	0.03	
ASA score [ref. = I]	II	1.11 [0.75, 1.66]	0.002	
	III-V	2.14 [1.32, 3.45]		
	Missing	1.15 [0.63, 2.11]		

As for QCI 1111 (overall survival), adjusted center effects are estimated from both a fixed effects outcome regression (i.e. from a Firth-corrected Cox regression model) and a hierarchical outcome regression (i.e. frailty Cox regression model). The hierarchical regression method encounters computational problems and does not provide reliable estimates for the center effects in this instance. Hence, these results are not further considered.

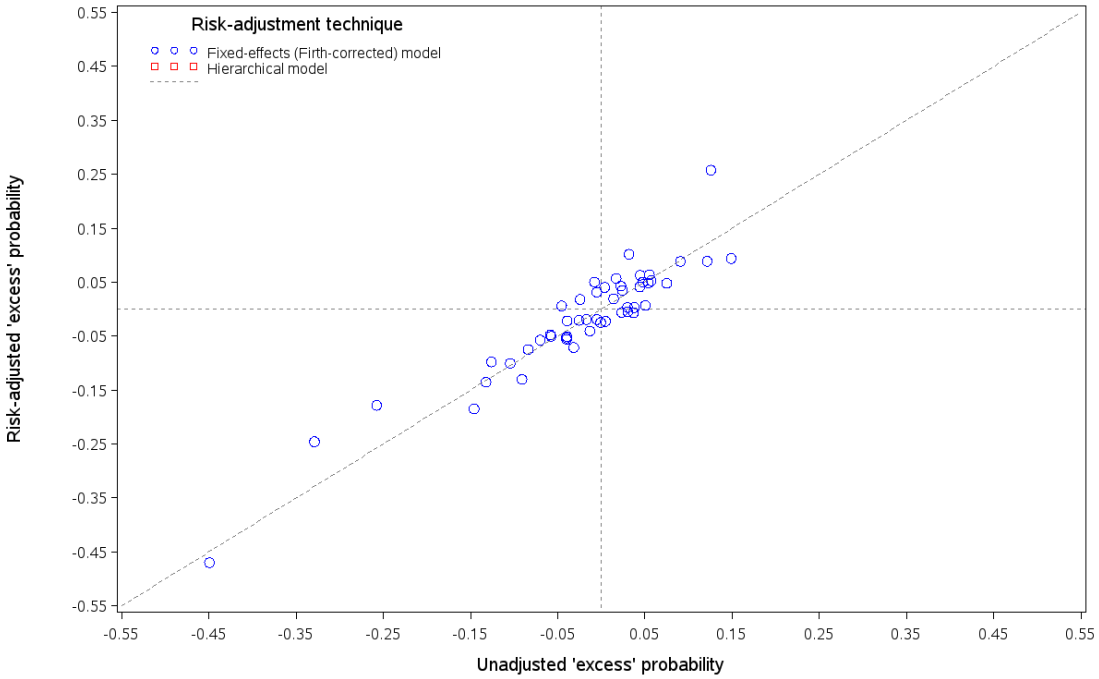
As described before, center effects are expressed as the 'excess' probability of 3-year survival relative to the 'average' center. A basic summary of the distribution of center effects as estimated from the unadjusted and (fixed-effects) adjusted analyses is presented in Table 67.

Table 67: Minimum, P25, P75, maximum and interquartile range of the center-effects (%) for QCI 1113b [DFS] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-45	-5	4	15	9
Fixed-effects regression	-47	-5	5	26	10

Figure 62 shows the relation between the adjusted and unadjusted center effects. From this we learn that the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects.

Figure 62: Scatter plot of adjusted center effects from fixed-effects outcome regression versus unadjusted center effects for QCI 1113b [DFS].



2.2 QUALITY INDICATORS RELATED TO DIAGNOSIS AND STAGING

2.2.1 Proportion of patients with a documented distance from the anal verge (QCI 1211, process)

2.2.1.1 Definition

N: Number of patients in denominator for whom lower limit of the tumor is known.

D: Number of registered patients.

Note that – probably due to a data management error – there are 10 patients in the PROCARE database with a missing lower limit of the primary tumor who are said to have a documented distance from the anal verge. This is not possible and corrected accordingly.

2.2.1.2 Description

Contrary to the definition in PROCARE II, where the denominator was restricted to patients undergoing resection, currently all patients are eligible for this QCI. Of the 3318 patients in the PROCARE database, 2999 (90%, or 89% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 19 (per size-grouped center) and Figure 9 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in one of the 69 (merged) centers to 100% in twenty-six of the (merged) centers. The funnel plot points to systematic variation between the centers.

2.2.1.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and ten prognostic factors, as shown in Table 68. For the prognostic factor ‘age’, the significant association is not with age itself, but with ‘missingness for age’. The separate associations of ‘BMI’ and ‘missingness for BMI’ are not significant, but jointly they are a strong prognostic factor for this QCI. The odds ratios for the ‘missing’ level for the other prognostic factors in Table 68 demonstrate a strong selection effect of missingness for these prognostic factors as well.

Table 69 describes the interpretation of the odds ratios obtained from univariate logistic regression models, such as those for QCI 1211 (Table 68) and all following QCIs.

Table 68: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1211 [%DocDist]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	1.00 [0.98, 1.01]	0.66	<0.0001
Missing Age [ref. = Not missing]	Missing	<0.001 [<0.001, 0.003]	<0.0001	
BMI	(continuous)	1.04 [0.97, 1.11]	0.27	< 0.0001
Missing BMI [ref. = Not missing]	Missing	0.22 [0.04, 1.19]	0.08	
ASA score [ref. = I]	II	0.80 [0.41, 1.54]	< 0.0001	
	III-V	0.29 [0.15, 0.56]		
	Missing	0.03 [0.02, 0.06]		
cStage [ref. = III]	I	0.81 [0.44, 1.48]	< 0.0001	
	II	0.89 [0.50, 1.59]		
	IV	0.32 [0.20, 0.50]		
	Missing / X	0.04 [0.03, 0.06]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	0.10 [0.05, 0.20]	< 0.0001	
	Missing	0.02 [0.01, 0.03]		
Ventral tumor [ref. = No]	Yes	1.77 [0.77, 4.08]	< 0.0001	
	Missing	0.03 [0.02, 0.05]		
cCRM positive [ref. = No]	Yes	0.39 [0.05, 3.17]	< 0.0001	
	Missing	0.05 [0.01, 0.34]		
cT4 [ref. = No]	Yes	0.41 [0.26, 0.63]	< 0.0001	
	Missing	0.04 [0.03, 0.05]		
Preoper. incontinence [ref. = No]	Yes	1.25 [0.64, 2.44]	< 0.0001	
	Missing	0.02 [0.01, 0.02]		
Surgical technique [ref. = PME]	TME	1.78 [1.11, 2.84]	< 0.0001	
	Missing	0.05 [0.03, 0.07]		

Table 69: Interpretation of the odds ratios obtained from univariate logistic regression models, illustrated using the results of Table 68.

Interpretation of the odds ratio for continuous covariates:

- For a BMI increase of 1 unit in the group of patients with a valid BMI, the odds (of having a documented distance from the anal verge) increases with a factor 1.04 ; the 95% confidence interval [0.97, 1.11] accounts for finite-sample imprecision. This effect should be considered together with the missingness indicator for BMI: for patients with missing BMI the odds are 0.22 times lower than for patients with a valid BMI.
- A similar interpretation holds for age, even though this is not a very good example for this particular QCI. For an age increase of 1 year in patients with a valid age, the odds (of having a documented distance from the anal verge) increase with a factor 1.00 (95% CI [0.98, 1.01]). This effect should be considered together with the missingness indicator for age: for patients with missing age the odds are less than 0.001 times that for a patient with valid age.

Interpretation of the odds ratios for a categorical covariate:

- E.g. for the ASA score: for patients with ASA score III, IV or V the odds (of having a documented distance from the anal verge) are 0.29 times those of patients with ASA score I (95% CI [0.15, 0.56]).

2.2.1.4 Estimation of unadjusted center effects

The unadjusted center effects are estimated from a (Firth-corrected) fixed effects logistic regression model and expressed as 'excess' probabilities (of having a documented distance from the anal verge). This 'excess' probability (relative to the average center) can be seen as the probability (of having a documented distance from the anal verge) associated with the specific center a patient was treated in.

Unadjusted center effects are shown in a caterpillar plot (Figure 9 in Section 1). These center effects range between -89% and 7% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -90% and 10% (since 90% of patients in the database achieved this QCI). The P25 and P75 are located at -8% resp. 4%, hence the interquartile range is 12%. In the caterpillar plot, we observe that seven (merged) centers perform significantly worse than P25, i.e. the upper bounds of their confidence intervals are lower than P25.

2.2.2 Proportion of patients in whom a CT of the abdomen and RX or CT thorax was performed before any treatment (QCI 1212, process)

2.2.2.1 Definition

N: Number of patients in denominator in whom an abdominal CT (for cT and/or cN staging) and RX or CT thorax (for cM staging) was performed before any treatment.
D: Number of patients who are registered directly in the online database and who underwent elective/scheduled surgery.

2.2.2.2 Description

There are 322 (or 10%) of the 3318 patients in the PROCARE database that meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 254 (79%, both weighted and unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 20 (per size-grouped center) and Figure 10 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in two of the 23 (merged) centers to 100% in eleven of the (merged) centers. The funnel plot points to systematic variation between the centers.

2.2.2.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and three prognostic factors, as shown in Table 70. The interpretation of the odds ratios is as described in Table 69. For the first two prognostic factors, the odds ratios for the 'missing' level demonstrate a strong effect of missingness for these prognostic factors.

Table 70: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1212 [%CT_Preop]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
cT4 [ref. = No]	Yes	0.68 [0.29, 1.61]	0.007
	Missing	0.23 [0.09, 0.58]	
Preoper. incontinence [ref. = No]	Yes	0.96 [0.35, 2.66]	0.0003
	Missing	0.10 [0.04, 0.31]	
Surgical technique [ref. = PME]	TME	2.63 [1.34, 5.15]	0.01
	Missing	0.59 [0.03, 9.99]	

2.2.2.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 10 in Section 1). These center effects range between -77% and 15% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -79% and 21% (since 79% of patients in the database achieved this QCI). The P25 and P75 are located at -10% resp. 12%, hence the interquartile range is 22%. In the caterpillar plot, we observe that three (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25.

2.2.3 Proportion of patients in whom a CEA was performed before any treatment (QCI 1213, process)

2.2.3.1 Definition

N: Number of patients in denominator for whom CEA serum level before treatment is reported.

D: Number of registered patients.

2.2.3.2 Description

All patients are eligible for this QCI. Of the 3318 patients in the PROCARE database, 2699 (81%, or 80% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 21 (per size-grouped center) and Figure 11 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in one of the 69 (merged) centers to 100% in six of the (merged) centers. The funnel plot points to systematic variation between the centers.

2.2.3.3 Identification of relevant prognostic factors

We find significant univariate associations between this QCI and eleven prognostic factors, as shown in Table 71. The interpretation of the odds ratios is as described in Table 69. For all prognostic factors, the odds ratios for the 'missing' level demonstrate a strong effect of missingness for these prognostic factors.

Table 71: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1213 [%CEA_Preop]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	0.99 [0.98, 1.00]	0.01	<0.0001
Missing Age [ref. = Not missing]	Missing	0.003 [0.001, 0.007]	<0.0001	
BMI	(continuous)	1.00 [0.97, 1.03]	0.98	<0.0001
Missing BMI [ref. = Not missing]	Missing	0.26 [0.12, 0.57]	0.0006	
Tumor level [ref. = Low]	Mid	0.99 [0.79, 1.26]	<0.0001	
	High	0.97 [0.71, 1.30]		
	Missing	0.06 [0.04, 0.08]		
ASA score [ref. = I]	II	1.45 [1.10, 1.91]	<0.0001	
	III-V	0.91 [0.67, 1.24]		
	Missing	0.21 [0.16, 0.27]		
cStage [ref. = III]	I	0.54 [0.39, 0.74]	<0.0001	
	II	0.83 [0.60, 1.16]		
	IV	0.65 [0.47, 0.90]		
	Missing / X	0.07 [0.06, 0.10]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	0.25 [0.14, 0.45]	<0.0001	
	Missing	0.13 [0.10, 0.16]		
Ventral tumor [ref. = No]	Yes	1.10 [0.84, 1.44]	<0.0001	
	Missing	0.20 [0.17, 0.25]		
cCRM positive [ref. = No]	Yes	0.76 [0.35, 1.62]	<0.0001	
	Missing	0.21 [0.11, 0.42]		
cT4 [ref. = No]	Yes	1.21 [0.84, 1.75]	<0.0001	
	Missing	0.09 [0.07, 0.11]		
Preoper. incontinence [ref. = No]	Yes	1.13 [0.82, 1.56]	<0.0001	
	Missing	0.06 [0.05, 0.08]		
Surgical technique [ref. = PME]	TME	1.32 [1.02, 1.71]	<0.0001	
	Missing	0.19 [0.14, 0.25]		

2.2.3.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 11 in Section 1). These center effects range between -79% and 15% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -81% and 19% (since 81% of patients in the database achieved this QCI). The P25 and P75 are located at -10% resp. 8%, hence the interquartile range is 18%. In the caterpillar plot, we observe that eight (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25. We also observe that three (merged) centers perform significantly above P75, i.e. the lower bounds of their confidence intervals are higher than P75.

2.2.4 Proportion of patients undergoing elective surgery that had preoperative complete large bowel-imaging (QCI 1214, process)

2.2.4.1 Definition

N: Number of patients in denominator who underwent a total colonoscopy or a complete double contrast enema or virtual colonoscopy.

D: Number of patients treated with elective or scheduled surgery.

2.2.4.2 Description

There are 2811 (or 85%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 2764 (98%, both weighted and unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 22 (per size-grouped center) and Figure 12 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 87% in one of the 68 (merged) centers to 100% in forty-eight of the (merged) centers. The funnel plot points to systematic variation between the centers.

2.2.4.3 Identification of relevant prognostic factors

We find significant univariate associations between this QCI and eight prognostic factors, as shown in Table 72. The interpretation of the odds ratios is as described in Table 69. For most prognostic factors, the odds ratios for the 'missing' level demonstrate a strong effect of missingness for these prognostic factors.

Table 72: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1214 [%Preop_Bowel_Im]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	1.00 [0.98, 1.03]	0.99	0.02
Missing Age [ref. = Not missing]	Missing	0.02 [<0.001, 0.42]	0.01	
BMI	(continuous)	1.04 [0.96, 1.14]	0.34	0.07
Missing BMI [ref. = Not missing]	Missing	1.57 [0.16, 15.51]	0.70	
Tumor level [ref. = Low]	Mid	0.93 [0.47, 1.83]	0.0004	
	High	0.97 [0.40, 2.36]		
	Missing	0.14 [0.05, 0.37]		
ASA score [ref. = I]	II	0.32 [0.12, 0.85]	0.08	
	III-V	0.30 [0.11, 0.87]		
	Missing	0.65 [0.16, 2.75]		
cStage [ref. = III]	I	1.82 [0.41, 8.00]	<0.0001	
	II	0.79 [0.31, 2.05]		
	IV	0.36 [0.16, 0.83]		
	Missing / X	0.17 [0.08, 0.35]		
Ventral tumor [ref. = No]	Yes	1.16 [0.56, 2.44]	0.06	
	Missing	0.47 [0.23, 0.94]		
cT4 [ref. = No]	Yes	0.81 [0.28, 2.33]	<0.0001	
	Missing	0.13 [0.07, 0.25]		
Preoper. incontinence [ref. = No]	Yes	1.79 [0.42, 7.63]	<0.0001	
	Missing	0.03 [0.01, 0.05]		

2.2.4.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 12 in Section 1). These center effects range between -12% and 2% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -98% and 2% (since 98% of patients in the database achieved this QCI). The P25 and P75 are located at -3% resp. 1%, hence the interquartile range is 4%. In the caterpillar plot, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

2.2.5 Use of TRUS in cT1/cT2 (new QCI 1214b, process)

2.2.5.1 Definition

N: Number of patients in denominator in whom cT was based on TRUS.

D: Number of patients with cT1 or cT2 rectal cancer, who underwent elective/scheduled surgery and are registered directly in the online database.

2.2.5.2 Description

There are 74 (or 2%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 61 (82%, or 81% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 23 (per size-grouped center) and Figure 13 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 50% in one of the 5 (merged) centers to 100% in two of the (merged) centers. The funnel plot does not point to systematic variation between the centers.

2.2.5.3 Identification of relevant prognostic factors

We find significant univariate association between this QCI and one prognostic factor, as shown in Table 73. The interpretation of the odds ratio is as described in Table 69. Note that while there is no association with BMI itself, the odds ratio for 'missing BMI' demonstrates a strong effect of missingness for the BMI covariate.

Table 73: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1214b [%TRUS_cT12]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Missing BMI [ref. = Not missing]	Missing	0.31 [0.09, 1.04]	0.06

2.2.5.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 13 in Section 1). These center effects range between -33% and 13% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -82% and 18% (since 82% of patients in the database achieved this QCI). The P25 and P75 are located at -15% resp. 10%, hence the interquartile range is 25%. In the caterpillar plot, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

2.2.6 Use of MRI in cStage II or III (new QCI 1214c, process)

2.2.6.1 Definition

N: Number of patients in denominator in whom cStaging was based on MRI.

D: Number of patients with cStage II or III rectal cancer based on any imaging technique, who underwent elective/scheduled surgery and are registered directly in the online database.

2.2.6.2 Description

There are 103 (or 3%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 94 (91%, or 89% unweighted) have achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 24 (per size-grouped center) and Figure 14 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 57% in one of the 10 (merged) centers to 100% in four (merged) centers. The funnel plot does not point to systematic variation between the centers.

2.2.6.3 Identification of relevant prognostic factors

We find significant univariate association between this QCI and one prognostic factor, as shown in Table 74. The interpretation of the odds ratio is as described in Table 69. Note that only two levels of cStage are considered, as a consequence of the QCI definition.

Table 74: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1214c [%MR_cII/III]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
cStage [ref. = III]	II	0.27 [0.06, 1.21]	0.09

2.2.6.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 14 in Section 1). These center effects range between -32% and 8% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -91% and 9% (since 91% of patients in the database achieved this QCI). The P25 and P75 are located at -13% resp. 6%, hence the interquartile range is 19%. In the caterpillar plot, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

2.2.7 Proportion of patients in whom a TRUS and pelvic CT and/or pelvic MRI was performed before any treatment (QCI 1215, process)

2.2.7.1 Definition

N: Number of patients in whom cT or cN were based on TRUS and at least one of the two following: pelvic CT and/or pelvic MRI.

D: Number of patients with rectal cancer of any stage and registered directly in the online database.

2.2.7.2 Description

There are 435 (or 13%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 264 (61%, or 57% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 25 (per size-grouped center) and Figure 15 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in three of the 26 (merged) centers to 100% in two (merged) centers. The funnel plot points to systematic variation between the centers.

2.2.7.3 Identification of relevant prognostic factors

We find significant univariate associations between this QCI and ten prognostic factors, as shown in Table 75. The interpretation of the odds ratios is as described in Table 69. For all prognostic factors, the odds ratios for the ‘missing’ level demonstrate a strong effect of missingness for these prognostic factors.

Table 75: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1215 [%Preop_Im]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
BMI	(continuous)	0.99 [0.93, 1.05]	0.75	<0.0001
Missing BMI [ref. = Not missing]	Missing	0.14 [0.03, 0.67]	0.01	
Tumor level [ref. = Low]	Mid	0.67 [0.39, 1.17]	<0.0001	
	High	0.73 [0.35, 1.53]		
	Missing	0.01 [0.01, 0.04]		
ASA score [ref. = I]	II	1.40 [0.77, 2.55]	<0.0001	
	III-V	1.39 [0.68, 2.85]		
	Missing	0.11 [0.06, 0.21]		
cStage [ref. = III]	I	1.12 [0.48, 2.60]	<0.0001	
	II	0.63 [0.28, 1.43]		
	IV	0.34 [0.19, 0.63]		
	Missing / X	0.06 [0.03, 0.11]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	0.49 [0.08, 3.01]	<0.0001	
	Missing	0.07 [0.04, 0.12]		
Ventral tumor [ref. = No]	Yes	2.06 [1.01, 4.19]	<0.0001	
	Missing	0.10 [0.06, 0.17]		
cCRM positive [ref. = No]	Yes	0.67 [0.17, 2.67]	<0.0001	
	Missing	0.14 [0.04, 0.45]		
cT4 [ref. = No]	Yes	0.43 [0.21, 0.88]	<0.0001	
	Missing	0.02 [0.01, 0.05]		
Preoper. incontinence [ref. = No]	Yes	0.76 [0.32, 1.81]	<0.0001	
	Missing	0.03 [0.01, 0.06]		
Surgical technique [ref. = PME]	TME	3.92 [2.10, 7.32]	<0.0001	
	Missing	0.17 [0.08, 0.39]		

2.2.7.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 15 in Section 1). These center effects range between -53% and 39% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -61% and 39% (since 61% of patients in the database achieved this QCI). The P25 and P75 are located at -26% resp. 24%, hence the interquartile range is 50%. In the caterpillar plot, we observe that three (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25. We also observe that one (merged) center performs significantly above P75, i.e. the lower bound of its confidence interval is higher than P75.

2.2.8 Proportion of patients with cStage II-III RC that have a reported cCRM (QCI 1216, process)

2.2.8.1 Definition

N: Number of patients in denominator for whom cCRM is reported.

D: Number of patients with cStage II-III treated with radical surgical resection.

2.2.8.2 Description

There are 1950 (or 59%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 501 (26%, or 19% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 26 (per size-grouped center) and Figure 16 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in twenty-one of the 63 (merged) centers to 78% in one (merged) center. The funnel plot points to systematic variation between the centers.

2.2.8.3 Identification of relevant prognostic factors

We find significant univariate associations between this QCI and eight prognostic factors, as shown in Table 76. The interpretation of the odds ratios is as described in Table 69. Note that only two levels of cStage are considered, as a consequence of the QCI definition.

Table 76: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1216 [%cCRM_rep]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	0.990 [0.981, 0.998]	0.02	0.06
Missing Age [ref. = Not missing]	Missing	<0.001 [<0.001, >999]	0.97	
BMI	(continuous)	0.96 [0.94, 0.99]	0.004	0.001
Missing BMI [ref. = Not missing]	Missing	0.29 [0.15, 0.58]	0.0005	
Gender [ref. = Male]	Female	0.75 [0.61, 0.93]	0.009	
Tumor level [ref. = Low]	Mid	1.01 [0.81, 1.25]	0.0002	
	High	0.49 [0.34, 0.70]		
	Missing	0.47 [0.21, 1.07]		
cStage [ref. = III]	II	0.34 [0.25, 0.45]	<0.0001	
Ventral tumor [ref. = No]	Yes	1.06 [0.84, 1.33]	0.002	
	Missing	0.54 [0.38, 0.78]		
Preoper. incontinence [ref. = No]	Yes	0.78 [0.57, 1.08]	0.07	
	Missing	0.52 [0.26, 1.03]		
Surgical technique [ref. = PME]	TME	2.36 [1.67, 3.33]	<0.0001	
	Missing	1.91 [0.87, 4.16]		

2.2.8.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 16 in Section 1). These center effects range between -12% and 64% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -26% and 74% (since 26% of patients in the database achieved this QCI). The P25 and P75 are located at -8% resp. 21%, hence the interquartile range is 29%. In the caterpillar plot, we observe that five (merged) centers perform significantly above P75, i.e. the lower bounds of their confidence intervals are higher than P75.

2.2.9 Accuracy of cM0 staging (new QCI 1216b, process)

2.2.9.1 Definition

N: Patients in denominator in whom no distant metastatic disease was diagnosed within 6 months following the date of first treatment (any type).

D: All patients with cStage I-III (as determined during staging and/or surgery) and for whom a 1 year follow-up is available.

2.2.9.2 Description

There are 634 (or 19%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 35 (6%, or 5% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 27 (per size-grouped center) and Figure 17 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in eighteen (merged) centers to 32% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

2.2.9.3 Identification of relevant prognostic factors

We find significant univariate associations between this QCI and six prognostic factors, as shown in Table 77. The interpretation of the odds ratios is as described in Table 69. For the prognostic factors BMI, ASA score, ventral tumor and surgical technique, the odds ratios for the 'missing' level demonstrate a strong effect of missingness for these prognostic factors. Note that only three levels of cStage are considered, as a consequence of the QCI definition

Table 77: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1216b [cM0_Acc]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age [ref. = < 70 years]	70+ years	0.51 [0.23, 1.12]	0.09
Missing BMI [ref. = Not missing]	Missing	2.06 [1.00, 4.26]	0.05
ASA score [ref. = I]	II	1.04 [0.42, 2.57]	0.05
	III-V	0.51 [0.13, 2.02]	
	Missing	2.88 [0.99, 8.34]	
cStage [ref. = III]	I	2.59 [1.16, 5.78]	0.06
	II	1.13 [0.44, 2.89]	
Ventral tumor [ref. = No]	Yes	1.36 [0.62, 2.98]	0.08
	Missing	2.78 [1.14, 6.75]	
Surgical technique [ref. = PME]	TME	1.42 [0.49, 4.15]	0.01
	Missing	7.85 [1.75, 35.2]	

2.2.9.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 17 in Section 1). These center effects range between -5% and 26% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -6% and 94% (since 6% of patients in the database achieved this QCI). The P25 and P75 are located at -2% resp. 4%, hence the interquartile range is 6%. In the caterpillar plot, we observe that one (merged) center performs significantly above P75, i.e. the lower bound of its confidence interval is higher than P75.

2.2.10 Time between first histopathological examination and first treatment (QCI 1217, process)

2.2.10.1 Definition

The time interval in days is computed between the date of pathologic diagnosis, if available, otherwise the date of first contact/hospitalization, and the date of first treatment.

D: All patients who underwent treatment (surgery and/or radiotherapy and/or chemotherapy) and for whom the date of biopsy or date of first consultation and the date of first treatment is known.

2.2.10.2 Description

Of the 3318 patients, 2687 (81%) are eligible for the denominator of this QCI. The 630 patients who are not eligible had either a missing date of biopsy or first consultation or a missing date of first treatment or both.

Overall, the time between the biopsy and first treatment ranges from 0 to 1109 days (or about 3 years). More detail on the distribution of this QCI is shown in Table 28 (per size-grouped center) and Figure 18 (a box plot per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1.

Note that in practice, waiting more than 1 month (30 days) to treat a patient with confirmed rectal cancer is not defendable. Nevertheless we observe about half of the patients with a longer time gap between diagnosis and first treatment. This is partly explained by the fact that for many patients in the PROCARE database the information on neoadjuvant treatment is not available, and for these patients surgery is considered as the 'first treatment'. It is quite likely, though, that many of these patients did receive some form of neoadjuvant treatment before surgery and hence the time between diagnosis and first treatment is then overestimated for them, see Table 78.

Table 78: Statistical summary of the time between histopathological diagnosis and first treatment, for patients eligible for QCI and separately for patients receiving neoadjuvant treatment (yes or no/unknown).

Neoadjuyant treatment	Distribution of time between histopathological diagnosis and first treatment								
	N patients	Minimum	Lower Quartile	Median	Upper Quartile	Maximum	Quartile Range	Mean	Std Dev
Yes	1628	0	19	27	39	493	20	34	33
No/unknown	1059	0	12	24	42	1109	30	41	68

Also note that there is a significant association between having had neoadjuvant treatment and being eligible for this QCI; patients for whom no neoadjuvant treatment was reported in the PROCARE database are less likely to be eligible for QCI 1217, see Table 79.

Table 79: Cross-tabulation of eligibility indicator for QCI 1217 versus neoadjuvant treatment received (yes or no/unknown) among all patients in the PROCARE database with cStage different from 0.

Neoadjuvant treatment	Eligible for QCI 1217		
Frequency Row Pct	No	Yes	Total
No/unknown	374 26.10	1059 73.90	1433
Yes	257 13.63	1628 86.37	1885
Total	631 19.02	2687 80.98	3318 100.00

As the upper boundary of 1109 days between histopathological diagnosis and first treatment is very large and far away from what is supposed to be common practice, we censor this QCI by setting all time intervals longer than 180 days equal to 180. Table 29 (per size-grouped center) and Figure 18 (a box plot per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1 show the distribution of the time intervals between histopathological examination and first treatment, per participating center for this censored QCI. From this we observe quite large differences between the centers concerning the length of the time interval between biopsy and first treatment.

2.2.10.3 Identification of relevant prognostic factors

We find significant univariate associations between this censored QCI and five prognostic factors, as shown in Table 80. The interpretation of the effects is as in Table 81.

Table 80: Estimated coefficients [95% confidence interval] and corresponding p-value from the univariate linear regression models for QCI 1217 [Time_histo-1ther], considering all patients in the PROCARE database. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Coefficient [95% CI]	*p*-value	Joint *p*-vaue
Age	(continuous)	-0.15 [-0.25, -0.05]	0.004	
BMI	(continuous)	-0.33 [-0.63, -0.04]	0.03	< 0.0001
Missing BMI [ref. = Not missing]	Missing	-14.19 [-22.25, -6.13]	0.0006	
Tumor level [ref. = Missing]	Low	-3.81 [-11.77, 4.15]	< 0.0001	
	Mid	-6.35 [-14.33, 1;63]		
	High	-12.83 [-21.08, -4.58]		
cStage [ref. = X/Missing]	I	0.79 [-4.47, 6.06]	0.004	
	II	-0.08 [-5.13, 4.96]		
	III	3.43 [-0.98, 7.83]		
	IV	7.73 [2.41, 13.05]		
Surgical technique [ref. = Missing]	TME	-0.87 [-6.34, 4.60]	< 0.0001	
	PME	-9.07 [-15.02, -3.12]		

Table 81: Interpretation of the coefficients obtained from univariate linear regression models, illustrated using the results of Table 80.

Interpretation of the estimated coefficients for continuous covariates:

- For a BMI increase of 1 unit in the group of patients with a valid BMI, the estimated time between histopathological examination and first treatment reduces on average with 0.33 days; the 95% confidence interval [-0.63, -0.04] accounts for finite-sample imprecision. This effect should be considered together with the missingness indicator for BMI: for patients with missing BMI this time gap is on average 14.19 days shorter than for patients with a valid BMI.
- A similar interpretation holds for age, for an age increase of 1 year, the time between histopathological examination and first treatment reduces on average with 0.15 days (95% CI [-0.25, -0.05]).

Interpretation of the estimated coefficients for a categorical covariate:

- E.g. for the tumor level: for patients with a high tumor (10-15 cm from the margo ani) the time between histopathological examination and first treatment is on average 12.83 days shorter than for patients with a missing tumor (95% CI [-21.08, -4.58]).

2.2.10.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 19 in Section 1). These center effects range between -24 and 41 ‘excess’ days between histopathological examination and first treatment. The P25 and P75 are located at -7 respectively 7 days, hence the interquartile range is 14%. In the caterpillar plot, we observe that three (merged) centers perform significantly above P75, i.e. the lower bound of their confidence interval is higher than P75, and one (merged) center performs significantly below P25, i.e. the upper bound of its confidence interval is lower than P25.

2.2.10.5 Accuracy of cT/cN staging if no or short radiotherapy (new QCI 1218)

2.2.10.6 Definition

For patients who did not receive neoadjuvant long course radio(chemo)therapy, the (y)pT respectively (y)pN is shown versus the cT respectively cN for these patients.

D: All patients with TRUS/CT/MRI with no or short neoadjuvant radiotherapy (without long R(C)T) and for whom the pT and pN is known and for whom the cT and cN is known (excluding patients with c and/or pTx and/or c and/or pNx).

2.2.10.7 Description

Note that the database does not allow to distinguish between patients who had no neoadjuvant radiotherapy and patients for whom it is not known whether (and which form of) they had neoadjuvant radiotherapy. Therefore, only patients with short-course neoadjuvant radiotherapy and known cN, cT, (y)pN and (y)pT are considered for this QCI.

For the accuracy of cT staging there are 204 patients eligible, i.e. patients who had short course radiotherapy and cT0, cT1, cT2, cT3 or cT4 and (y)pT0, (y)pT1, (y)pT2, (y)pT3 or (y)pT4. The two-way frequency table of cT versus (y)pT is given in Table 82.

Table 82: Two-way frequency table of cT versus (y)pT in patients who had short course neoadjuvant radiotherapy and have a known cT and (y)pT stage.

Frequency Row Pct		(y)pT					Total
		T0	T1	T2	T3	T4	
cT	T2	1 2.63	4 10.53	19 50.00	13 34.21	1 2.63	38
	T3	1 0.63	5 3.14	39 24.53	107 67.30	7 4.40	159
	T4	0 0.00	0 0.00	1 14.29	4 57.14	2 28.57	7
Total		2	9	59	124	10	204

From Table 82 we observe a strong association between cT and (y)pT (X^2-test statistic = 26.87, *p*-value = 0.0007), and most confusion between T2 and T3 stagings.

For the accuracy of cN staging there are 204 patients eligible, i.e. patients who had short course radiotherapy and cN0, cN1 or cN2 and (y)pN0, (y)pN1 or (y)pN2. The two-way frequency table of cN versus (y)pN is given in Table 83.

Table 83: Two-way frequency table of cN versus (y)pN in patients who had short course neoadjuvant radiotherapy and have a known cN and (y)pN stage.

Frequency Row Pct		(y)pN			Total
		N0	N1	N2	
cN	N0	60 65.22	21 22.83	11 11.96	92
	N1	44 50.57	23 26.44	20 22.99	87
	N2	8 32.00	8 32.00	9 36.00	25
Total		112	52	40	204

From Table 83 we observe a significant association between cN and (y)pN (X^2-test statistic = 11.85, *p*-value = 0.02), but still a fair amount of 'misclassification', even between node-positive versus node-negatives.

No further statistical analyses are performed for this QCI.

2.3 QUALITY INDICATORS RELATED TO NEOADJUVANT TREATMENT

2.3.1 Proportion of cStage II-III patients that received a neoadjuvant pelvic RT (new QCI 1221, process)

2.3.1.1 Definition

N: Number of patients in denominator who received neoadjuvant radio(chemo)therapy.

D: Number of patients in cStage II or III, treated with radical surgical resection with rectal cancer at any level and for whom the course of radiotherapy treatment is not missing.

Note that there is also a version of this QCI for patients with 1) high RC, 2) mid RC and 3) low RC. In this report we only focus on the global version.

Note that this QCI (like some other QCIs in this domain) is highly unreliable since the database does not allow to distinguish between the 1442 (43% of the patients in the PROCARE database) patients who were not treated and patients for whom the treatment information is missing. *All these patients should be excluded from the denominator of this QCI*.

2.3.1.2 Description

There are 1830 (or 55%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 1360 (74%, or 70% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 30 (per size-grouped center) and Figure 20 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in one of the 61 (merged) centers to 100% in three (merged) centers. The funnel plot points to systematic variation between the centers.

2.3.1.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and eleven prognostic factors, as shown in Table 84. The interpretation of the odds ratios is as described in Table 69. Note that only two levels of cStage are considered, as a consequence of the QCI definition.

2.3.1.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 20 in Section 1). These center effects range between -66% and 25% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -70% and 30% (since the average center achievement is at 70% for this QCI). The P25 and P75 are located at -14% resp. 13%, hence the interquartile range is 27%. In the caterpillar plot, we observe that five (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25. We also observe that one (merged) center performs significantly above P75, i.e. the lower bound of its confidence interval is higher than P75.

Table 84: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1221 [%Preop_RT]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	0.96 [0.95, 0.97]	<0.0001	< 0.0001
Missing Age [ref. = Not missing]	Missing	>999 [<0.001, >999]	0.98	
BMI	(continuous)	1.00 [0.97, 1.03]	0.96	0.01
Missing BMI [ref. = Not missing]	Missing	0.69 [0.35, 1.38]	0.29	
Gender [ref. = Male]	Female	0.65 [0.53, 0.81]	<0.0001	
Tumor level [ref. = Low]	Mid	0.68 [0.52, 0.87]	<0.0001	
	High	0.15 [0.11, 0.20]		
	Missing	0.49 [0.25, 0.95]		
ASA score [ref. = I]	II	1.01 [0.77, 1.33]	<0.0001	
	III-V	0.50 [0.37, 0.68]		
	Missing	0.63 [0.43, 0.92]		
cStage [ref. = III]	II	0.41 [0.33, 0.52]	<0.0001	
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	0.12 [0.04, 0.33]	<0.0001	
	Missing	0.57 [0.29, 1.11]		
Ventral tumor [ref. = No]	Yes	1.29 [1.00, 1.66]	0.0002	
	Missing	0.63 [0.47, 0.85]		
cCRM positive [ref. = No]	Yes	1.62 [0.89, 2.94]	<0.0001	
	Missing	0.45 [0.27, 0.75]		
Preoper. incontinence [ref. = No]	Yes	0.62 [0.46, 0.84]	0.005	
	Missing	1.22 [0.64, 2.33]		
Surgical technique [ref. = PME]	TME	4.33 [3.33, 5.63]	<0.0001	
	Missing	3.60 [1.65, 7.87]		

2.3.2 Proportion of patients with cCRM ≤ 2 mm on MRI/CT that received long course neoadjuvant radio(chemo)therapy (new QCI 1221b, process)

2.3.2.1 Definition

N: Number of patients in denominator who received long course neoadjuvant radio(chemo)therapy.

D: Number of patients treated with radical surgical resection and for whom cCRM is ≤ 2 mm and for whom it is known whether they received neoadjuvant treatment or not.

2.3.2.2 Description

There are 286 (or 9%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 231 (81%, or 76% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 31 (per size-grouped center) and Figure 21 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1.

This proportion ranges from 40% in two of the 15 (merged) centers to 99% in one (merged) center. The funnel plot points to systematic variation between the centers.

2.3.2.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and five prognostic factors, as shown in Table 85. The interpretation of the odds ratios is as described in Table 69. For ASA score and preoperative incontinence, the odds ratios for the 'missing' level demonstrate a strong effect of missingness for these prognostic factors.

Table 85: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1221b [%(C)RT_cCRM+]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age	(continuous)	0.96 [0.93, 0.98]	0.002
Gender [ref. = Male]	Female	0.50 [0.28, 0.91]	0.02
ASA score [ref. = I]	II	0.35 [0.13, 0.94]	0.04
	III-V	0.21 [0.07, 0.61]	
	Missing	0.44 [0.11, 1.80]	
cStage [ref. = III]	I	0.05 [0.01, 0.47]	0.10
	II	0.73 [0.26, 2.09]	
	IV	0.64 [0.26, 1.60]	
	Missing / X	0.61 [0.06, 6.02]	
Preoper. incontinence [ref. = No]	Yes	0.48 [0.22, 1.01]	0.06
	Missing	0.20 [0.03, 1.49]	

2.3.2.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 21 in Section 1). These center effects range between -38% and 17% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -81% and 19% (since 81% of patients in the database achieved this QCI). The P25 and P75 are located at -14% resp. 13%, hence the interquartile range is 27%. In the caterpillar plot, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

2.3.3 Proportion of patients with cStage I that received neoadjuvant radio(chemo)therapy (new QCI 1221c, process)

2.3.3.1 Definition

N: Number of patients in denominator who received neoadjuvant R(C)T.

D: Number of patients treated with radical surgical resection for cStage I rectal cancer.

Note that there is also a version of this QCI for patients with 1) high RC, 2) mid RC and 3) low RC. In this report we only focus on the global version.

2.3.3.2 Description

There are 344 (or 10%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 60 (17%, or 16% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 32 (per size-grouped center) and Figure 22 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in twelve of the 28 (merged) centers to 66% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

Note that, since also patients for whom it is not known whether they received neoadjuvant treatment or not are included in the denominator, this QCI provides a lower limit for the proportion of patients with cStage I that received neoadjuvant radio(chemo)therapy.

2.3.3.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and two prognostic factors, as shown in Table 86. The interpretation of the odds ratios is as described in Table 69. For surgical technique, the odds ratio for the 'missing' level demonstrates a very strong effect of missingness for this prognostic factor.

Table 86: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1221c [%Preop_RT_cl]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
BMI	(continuous)	0.98 [0.91, 1.06]	0.63	0.04
Missing BMI [ref. = Not missing]	Missing	0.26 [0.03, 2.23]	0.22	
Surgical technique [ref. = PME]	TME	2.26 [1.06, 4.81]	0.02	
	Missing	18.44 [1.52, 224]		

2.3.3.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 22 in Section 1). These center effects range between -11% and 49% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -17% and 83% (since 17% of patients in the database achieved this QCI). The P25 and P75 are located at -8% resp. 10%, hence the interquartile range is 18%. In the caterpillar plot, we

observe that there are no (merged) centers that perform significantly below P25 or above P75.

2.3.4 Proportion of cStage II-III patients treated with neoadjuvant 5-FU based chemoradiation, that received a continuous infusion of 5-FU (QCI 1224, process)

2.3.4.1 Definition

N: Number of patients in denominator that received a continuous infusion of 5-FU.

D: Number of patients with cStage II-III treated with radical surgical resection and long course pelvic chemoradiotherapy.

2.3.4.2 Description

There are 469 (or 14%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 425 (91%, both weighted and unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 33 (per size-grouped center) and Figure 23 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 12% in one of the 31 (merged) center to 100% in twenty-one (merged) centers. The funnel plot points to systematic variation between the centers.

2.3.4.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and three prognostic factors, as shown in Table 87. The interpretation of the odds ratios is as described in Table 69. Note that only two levels of cStage are considered, as a consequence of the QCI definition.

Table 87: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1224 [%Preop_cont_5FU]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
BMI	(continuous)	1.21 [1.03, 1.22]	0.01	0.03
Missing BMI [ref. = Not missing]	Missing	24.2 [2.3, 252]	0.008	
ASA score [ref. = I]	II	0.25 [0.09, 0.73]	0.05	
	III-V	0.24 [0.07, 0.86]		
	Missing	0.86 [0.09, 8.05]		
cStage [ref. = III]	II	0.46 [0.22, 0.95]	0.04	

2.3.4.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 23 in Section 1). These center effects range between -75% and 7% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -91% and 9% (since 9% of patients in the database achieved this QCI). The P25 and P75 are located at -3% resp. 4%, hence the interquartile range is 7%. In the caterpillar plot, we observe that three (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25.

2.3.5 Proportion of cStage II-III patients treated with a long course of preoperative pelvic RT or chemoradiation, that completed this neoadjuvant treatment within the planned timing (QCI 1225, process)

2.3.5.1 Definition

N: Number of patients in denominator for whom the radiotherapy treatment was not interrupted for more than five working days.

D: Number of patients with cStage II-III who started with long course neoadjuvant radiotherapy which was followed by radical surgical resection.

2.3.5.2 Description

There are 1196 (or 36%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 1158 (97%, both weighted and unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 34 (per size-grouped center) and Figure 24 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 60% in one of the 52 (merged) centers to 100% in thirty-four (merged) centers. The funnel plot points to systematic variation between the centers.

2.3.5.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and six prognostic factors, as shown in Table 88. The interpretation of the odds ratios is as described in Table 69. For all prognostic factors except age, the odds ratios for the 'missing' level demonstrate a strong effect of missingness for these prognostic factors.

Table 88: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1225 [%Completed_preop_RT]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age	(continuous)	1.03 [1.00, 1.06]	0.05
Tumor level [ref. = Low]	Mid	1.75 [0.80, 3.86]	0.007
	High	0.91 [0.31, 2.69]	
	Missing	0.19 [0.06, 0.59]	
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	0.03 [0.004, 0.20]	< 0.0001
	Missing	0.09 [0.03, 0.25]	
Ventral tumor [ref. = No]	Yes	1.08 [0.48, 2.41]	0.01
	Missing	0.33 [0.15, 0.73]	
Preoper. incontinence [ref. = No]	Yes	0.71 [0.27, 1.86]	0.004
	Missing	0.18 [0.07, 0.49]	
Surgical technique [ref. = PME]	TME	0.55 [0.13, 2.33]	0.003
	Missing	0.09 [0.02, 0.50]	

2.3.5.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 24 in Section 1). These center effects range between -35% and 3% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -97% and 3% (since 97% of patients in the database achieved this QCI). The P25 and P75 are located at -3% resp. 2%, hence the interquartile range is 5%. In the caterpillar plot, we observe that one (merged) center performs significantly below P25, i.e. the upper bound of its confidence interval is lower than P25.

2.3.6 Proportion of cStage II-III patients treated with a long course of preoperative pelvic RT or chemoradiation, that was operated 4 to 12 weeks after completion of the (chemo)radiation (QCI 1226, process)

2.3.6.1 Definition

N: Number of patients in denominator that was operated 4 to 12 weeks after completion of the (chemo)radiotherapy.

D: Number of patients with cStage II-III treated with long course neoadjuvant radiotherapy and for whom date of surgery and date of last irradiation are not missing.

2.3.6.2 Description

There are 1123 (or 34%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 1094 (97%, or 98% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 35 (per size-grouped center) and Figure 25 (per participating center, after merging all centers with less than five

eligible patients in one overlapping center) in Section 1. This proportion ranges from 86% in one of the 50 (merged) centers to 100% in thirty-three (merged) centers. The funnel plot does not point to systematic variation between the centers.

2.3.6.3 Univariate associations with prognostic factors

We find no significant univariate association between this QCI and any of the candidate prognostic factors.

2.3.6.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 25 in Section 1). These center effects range between -14% and 3% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -97% and 3% (since 97% of patients in the database achieved this QCI). The P25 and P75 are located at -3% resp. 2%, hence the interquartile range is 5%. In the caterpillar plot, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

2.3.7 *Rate of acute grade 4 radio(chemo)therapy-related complications (QCI 1227, outcome)

2.3.7.1 Definition

N: Number of patients in denominator that presented acute grade 4 complications during the interval until surgery for neoadjuvant (chemo)radiotherapy or as mentioned in the first follow-up for adjuvant (chemo)radiotherapy.

D: Number of patients treated with neoadjuvant or adjuvant radiotherapy and for whom date of surgery in case of neoadjuvant (chemoradiotherapy) and/or follow-up data are available in case of adjuvant radio(chemo)therapy.

2.3.7.2 Description

Note that – contrary to most other QCIs - fulfilling this QCI is not a positive event.

There are 544 patients of the 3318 (16%) patients in the PROCARE database eligible for this QCI. Of the 544 patients eligible for this QCI, 62 (11%, both weighted and unweighted) showed acute grade 4 radio(chemo)therapy-related complications. The proportion of patients that achieved the QCI is shown in Table 36 (per size-grouped center) and Figure 26 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 9 of the 31 (merged) centers to 30% in one (merged) centers. The funnel plot does not point to systematic variation between the centers.

2.3.7.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the prognostic factor BMI is suggested to be used for risk-adjustment.

Empirical associations

We find significant univariate associations between this QCI and two prognostic factors, as shown in Table 89. The interpretation of the odds ratios is as described in Table 69.

Table 89: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1227 [%grade4_Tox_Preop_RT]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age	(continuous)	1.03 [1.00, 1.06]	0.03
ASA score [ref. = I]	II	1.12 [0.57, 2.21]	0.07
	III-V	1.21 [0.46, 3.21]	
	Missing	3.08 [1.23, 7.67]	

2.3.7.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 27 in Section 1).

Unadjusted center effects range between -9% and 20% 'excess' probability of acute grade 4 radio(chemo)therapy-related complications. Note that the 'excess probabilities' are automatically constrained between -11% and 89% (since 11% of patients in the database achieved this QCI). The P25 and P75 are located at -5% respectively 10%, hence the interquartile range is 15%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of acute grade 4 radio(chemo)therapy-related complications. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cStage and level of the tumor (high, mid or low) were considered.

A model with main effects for age and gender was retained. The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 90 and interpreted in Table 91.

Table 90: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1227 [%grade4_Tox_Preop_RT]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age	(continuous)	1.03 [1.00, 1.05]	0.05
Gender [ref. = Male]	Female	1.23 [0.71, 2.11]	0.46

Table 91: Interpretation of the odds ratios obtained from multivariate logistic regression models, illustrated using the results of Table 90.

Interpretation of the odds ratio for continuous covariates:

- Per age increase of 1 year in the group of patients with a valid age *and the same gender*, the odds (of having acute grade 4 radio(chemo)therapy-related complications) increase with a factor 1.03 (95% CI [1.00, 1.05]).

Interpretation of the odds ratios for a categorical covariate:

- E.g. for gender: for female patients the odds (of having acute grade 4 radio(chemo)therapy-related complications) are 1.23 times those of male patients *with the same age* (95% CI [0.71, 2.11]).

Adjusted center effects are estimated from a Firth-corrected logistic regression model, from a hierarchical logistic regression model, and from the doubly robust propensity score method as described in Section 1. As described before, center effects are the 'excess' probabilities of grade 4 radio(chemo)therapy-related complications, relative to the 'average' center.

Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 27 in Section 1). Table 92 contains a basic summary of the distribution of the center effects as obtained from the fixed-effects regression, hierarchical regression and doubly-robust method. In the two caterpillar plots (unadjusted and adjusted) in Figure 27 in Section 1, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

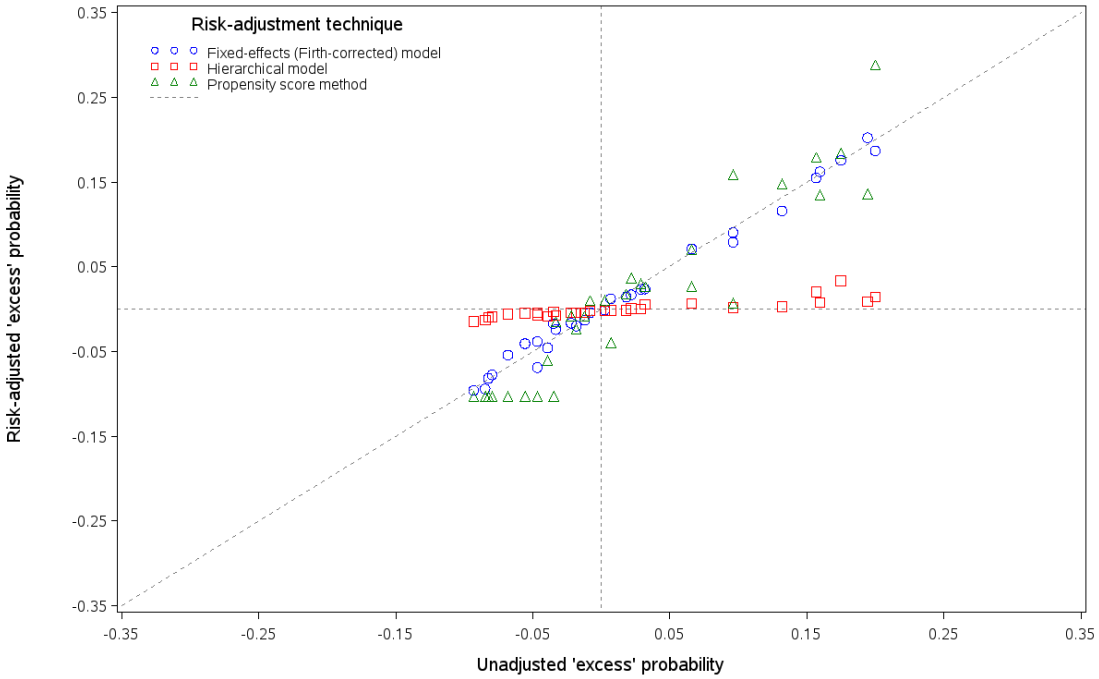
Table 92: Minimum, P25, P75, maximum and interquartile range (%) of the center-effects for QCI 1227 [%grade4_Tox_Preop_RT] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-9	-5	10	20	15
Fixed-effects regression	-10	-4	8	20	12
Hierarchical regression	-1	-0.5	0.5	3	1
Doubly-robust method	-10	-10	5	29	16

Figure 63 shows the relation between the adjusted and unadjusted center effects. From this we learn the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects and that the center effects obtained from the hierarchical model are strongly shrunken towards zero. The doubly-robust propensity score method in this instance provides center effects that also stay generally close to the unadjusted center effects.

Note that for the 9 of the 31 centers in which no grade 4 radio(chemo)therapy-related complications occurred, the population-averaged probability of grade 4 radio(chemo)therapy-related complications is automatically set to zero and therefore the 'excess' probability to -10%, see also Figure 63.

Figure 63: Scatter plot of adjusted center effects (from fixed-effects outcome regression, random effects outcome regression and the doubly –robust propensity score method) versus unadjusted center effects for QCI 1227 [%grade4_Tox_Preop_RT].



2.4 QUALITY INDICATORS RELATED TO SURGERY

2.4.1 *Proportion of R0 resections (QCI 1231, outcome)

2.4.1.1 Definition

N: Number of patients in denominator with R0 resection.

D: Number of patients treated with radical surgical resection and for whom R status is not missing.

Note that – like in PROCARE II [1] – the denominator was additionally restricted such that all cStage IV patients automatically become not eligible for this QCI. The rationale behind this decision is that cStage IV patients can in practice not have a complete resection since they have secondary tumors in other organs than the rectum.

2.4.1.2 Description

There are 2576 of the 3318 (78%) patients in the PROCARE database eligible for this QCI. Of the 2576 patients eligible for this QCI, 2230 (87%, or 86% unweighted) had an R0 resection. The proportion of patients that achieved the QCI is shown in Table 37 (per size-grouped center) and Figure 28 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 40% in one of the 68 (merged) centers to 100% in 11 (merged) centers. The funnel plot points to systematic variation between the centers.

2.4.1.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus no prognostic factors were identified for this QCI, but clinical experts suggested to use cT4 (yes or no) instead of cStage as prognostic factor.

Empirical associations

We find significant (*p*-value < 0.10) univariate associations between this QCI and six prognostic factors, as shown in Table 93. The interpretation of the odds ratios is as described in Table 69.

Table 93: Odds ratio [95% Wald confidence interval] estimate and corresponding p-value from the univariate logistic regression models for QCI 1231 [%R0res]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age	(continuous)	0.99 [0.98, 1.00]	0.05
Gender [ref. = Male]	Female	0.76 [0.60, 0.95]	0.02
cStage [ref. = III]	0/I	2.46 [1.56, 3.88]	0.0003
	II	0.97 [0.72, 1.31]	
	Missing/X	0.79 [0.56, 1.11]	
Tumor level [ref. = Low]	Mid	1.47 [1.14, 1.90]	0.005
	High	1.56 [1.10, 2.20]	
	Missing	0.88 [0.48, 1.61]	
cT4 [ref. = No]	Yes	0.30 [0.22, 0.41]	<0.0001
	Missing	0.61 [0.41, 0.92]	
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	0.37 [0.18, 0.78]	0.02
	Missing	1.51 [0.65, 3.53]	

2.4.1.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 29 in Section 1).

Unadjusted center effects range between -45% and 12% 'excess' probability of R0 resections. Note that the 'excess probabilities' are automatically constrained between -87% and 13% (since 87% of patients in the database achieved this QCI). The P25 and P75 are located at -7% respectively 5%, hence the interquartile range is 12%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of R0 resections. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cT4 and level of the tumor (high, mid or low) were considered.

A model with a missingness indicator for age, age itself, gender, tumor level and cT4 as main effects was retained. The final model also contains a significant interaction between age and cT4 (*p*-value = 0.0285). The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 94 and interpreted as in Table 91.

Table 94: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1231 [%R0res].
For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	0.99 [0.98, 1.00]	0.03	0.08
Missing Age [ref. = Not missing]	Missing	0.24 [0.03, 2.12]	0.20	
Gender [ref. = Male]	Female	0.80 [0.63, 1.02]	0.07	
Tumor level [ref. = Low]	Mid	1.40 [1.07, 1.83]	0.02	
	High	1.37 [0.96, 1.97]		
	Missing	0.64 [0.32, 1.28]		
cT4 [ref. = No]	Yes	0.05 [0.01, 0.27]	0.002	
	Missing	2.24 [0.14, 35.49]		
cT4 – Missing Age interaction [ref. = No, Not missing]	Missing, Missing	4.80 [0.05, 446.38]	0.50	0.03
cT4 – Age interaction [ref. = No cT4, (cont.)]	Yes, (cont.)	1.03 [1.00, 1.06]	0.04	
	Missing, (cont.)	0.98 [0.94, 1.02]	0.30	

Adjusted center effects are estimated from a Firth-corrected logistic regression model and a hierarchical logistic regression model. Center effects are the center-specific 'excess' probabilities of R0 resections, relative to the 'average' center.

Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 29 in Section 1). Table 95 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and from the fixed-effects and hierarchical outcome regression.

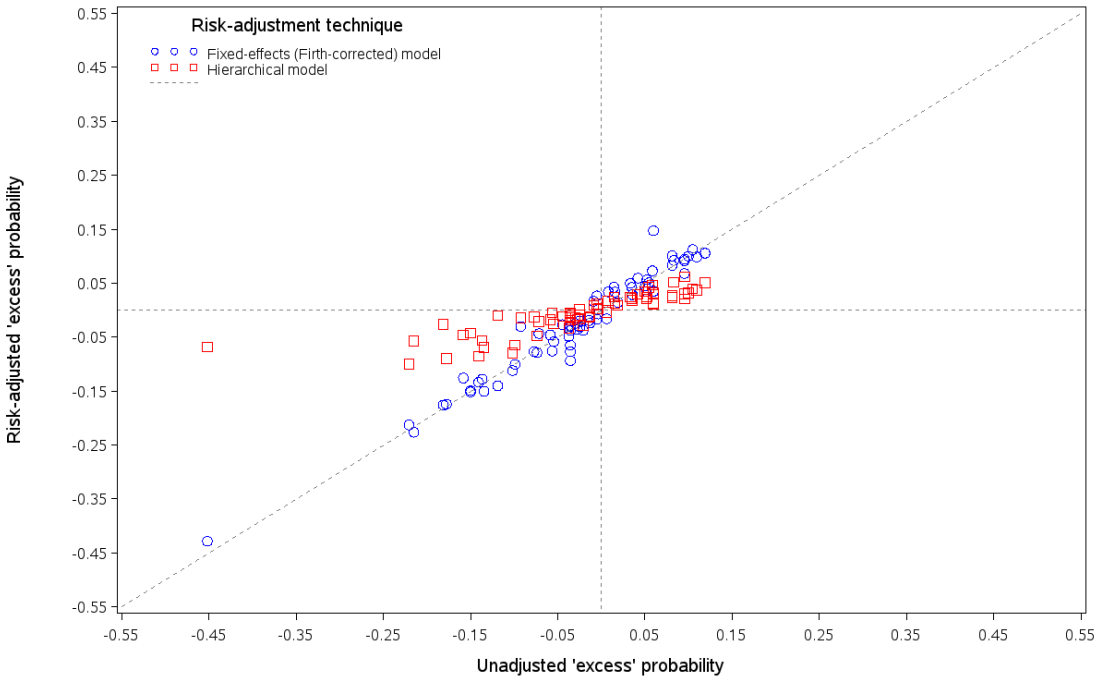
In the two caterpillar plots (unadjusted and adjusted) in Figure 29 in Section 1, we observe that there are two (merged) centers that perform significantly better than P75.

Table 95: Minimum, P25, P75, maximum and interquartile range (%) of the center-effects for QCI 1231 [%R0res] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-45	-7	5	12	12
Fixed-effects regression	-43	-8	4	15	12
Hierarchical regression	-10	-2	2	6	4

Figure 64 shows the relation between the adjusted and unadjusted center effects. From this we learn the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects and that there is some shrinkage in results obtained from the hierarchical approach.

Figure 64: Scatter plot of adjusted center effects (from both fixed- and hierarchical outcome regression) versus unadjusted center effects for QCI 1231 [%R0res].



2.4.2 Proportion of APER, Hartmann's procedure or total excision of colon and rectum with definitive ileostomy (QCI 1232a, process)

2.4.2.1 Definition

N: Number of patients in denominator in whom APER or Hartmann's procedure or total excision of colon and rectum with definitive ileostomy was performed.

D: Number of patients treated with any type of resection for rectal cancer at any known level.

Note that there is also a version of this QCI for patients with 1) high RC, 2) mid RC and 3) low RC. In this report we only focus on the global version.

2.4.2.2 Description

There are 2945 (or 89%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 703 (24%, or 26% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 38 (per size-grouped center) and Figure 30 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in two of the 68 (merged) centers to 78% in one (merged) center. The funnel plot points to systematic variation between the centers.

2.4.2.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and eleven prognostic factors, as shown in Table 96. The interpretation of the odds ratios is as described in Table 69. Note the very high odds ratios for surgical technique.

Table 96: Odds ratio estimate [95% confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1232a [%Defin_ostomy].

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	1.02 [1.02, 1.03]	<0.0001	<0.0001
Missing Age [ref. = Not missing]	Missing	2.18 [0.45, 10.52]	0.33	
BMI	(continuous)	0.98 [0.96, 1.00]	0.08	0.07
Missing BMI [ref. = Not missing]	Missing	0.69 [0.38, 1.26]	0.23	
Tumor level [ref. = Low]	Mid	0.10 [0.08, 0.12]	<0.0001	
	High	0.06 [0.04, 0.09]		
	Missing	0.39 [0.25, 0.61]		
ASA score [ref. = I]	II	1.15 [0.92, 1.44]	<0.0001	
	III-V	1.98 [1.53, 2.55]		
	Missing	1.39 [1.02, 1.88]		
cStage [ref. = III]	I	0.61 [0.45, 0.82]	<0.0001	
	II	1.34 [1.06, 1.68]		
	IV	1.24 [0.95, 1.62]		
	Missing / X	0.83 [0.61, 1.12]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	1.93 [1.08, 3.43]	0.0005	
	Missing	0.36 [0.19, 0.68]		
Ventral tumor [ref. = No]	Yes	1.32 [1.09, 1.60]	<0.0001	
	Missing	0.56 [0.43, 0.74]		
cCRM positive [ref. = No]	Yes	2.38 [1.46, 3.88]	0.002	
	Missing	1.86 [1.19, 2.93]		
cT4 [ref. = No]	Yes	3.93 [3.05, 5.06]	<0.0001	
	Missing	0.73 [0.50, 1.05]		
Preoper. incontinence [ref. = No]	Yes	2.18 [1.73, 2.74]	<0.0001	
	Missing	0.65 [0.40, 1.06]		
Surgical technique [ref. = PME]	TME	74.9 [24.0, 233.5]	<0.0001	
	Missing	138.6 [42.0, 458.1]		

2.4.2.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 30 in Section 1). These center effects range between -22% and 50% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -24% and 76% (since 24% of patients in the database achieved this QCI). The P25 and P75 are located at -8% resp. 11%, hence the interquartile range is 19%. In the caterpillar plot, we observe that one (merged) center performs significantly below P25, i.e. the upper bound of its confidence interval is lower than P25. We also observe that one (merged) center performs significantly above P75, i.e. the lower bound of its confidence interval is higher than P75.

2.4.3 *Proportion of patients with stoma 1 year after sphincter-sparing surgery (QCI 1232b, outcome)

2.4.3.1 Definition

N: Number of patients in denominator still having a stoma 1 year after surgery.

D: Number of patients treated with TME (complete rectum resection (TME) + straight CAA, coloplasty, pouch, side-to-end CAA, total excision of colon and rectum with IPAA, or another specified type of reconstruction) with a primary (constructed at the time of SSO) or secondary (constructed after SSO) derivative stoma or dismantling of anastomosis still alive 1 year after surgery and for whom follow-up at 1 year or more is known.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

2.4.3.2 Description

There are only 123 of the 3318 (4%) patients in the PROCARE database eligible for this QCI. Of these 123 patients, 33 (27%, or 25% unweighted) had a stoma 1 year after sphincter-sparing surgery. The proportion of patients that achieved the QCI is shown in Table 39 (per size-grouped center) and Figure 31 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in three of the 10 (merged) centers to 50% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

2.4.3.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors for were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the ASA co-morbidity score is identified as possible prognostic factor for this QCI.

Empirical associations

We find a significant (p-value < 0.10) univariate association between this QCI and age, as shown in Table 93. The interpretation of the odds ratios is as described in Table 69.

Table 97: Odds ratio [95% Wald confidence interval] estimate and corresponding p-value from the univariate logistic regression models for QCI 1232b [%stoma1year].

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age	(continuous)	0.96 [0.93, 1.00]	0.04

2.4.3.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 32 in Section 1).

Unadjusted center effects range between -18% and 28% 'excess' probability of having a stoma 1 year after sphincter-sparing surgery. Note that the 'excess probabilities' are automatically constrained between -27% and 73% (since 27% of patients in the database achieved this QCI). The P25 and P75 are located at -16% respectively 20%, hence the interquartile range is 36%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of patients having a stoma 1 year after sphincter-sparing surgery. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cStage and level of the tumor (high, mid or low) were considered.

A model with only the minimal set of prognostic factors (age and gender) was retained. There is no significant interaction between age and gender. The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 98 and interpreted as in Table 91.

Table 98: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1232b [%stoma1year].
For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age	(continuous)	0.96 [0.92, 1.00]	0.03
Gender [ref. = Male]	Female	1.82 [0.73, 4.51]	0.20

Adjusted center effects are estimated from a Firth-corrected logistic regression model and a hierarchical logistic regression model. Center effects are the center-specific 'excess' probabilities of having a stoma 1 year after sphincter-sparing surgery, relative to the 'average' center.

Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 32 in Section 1). Table 99 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and from the fixed-effects and hierarchical outcome regression. In the two

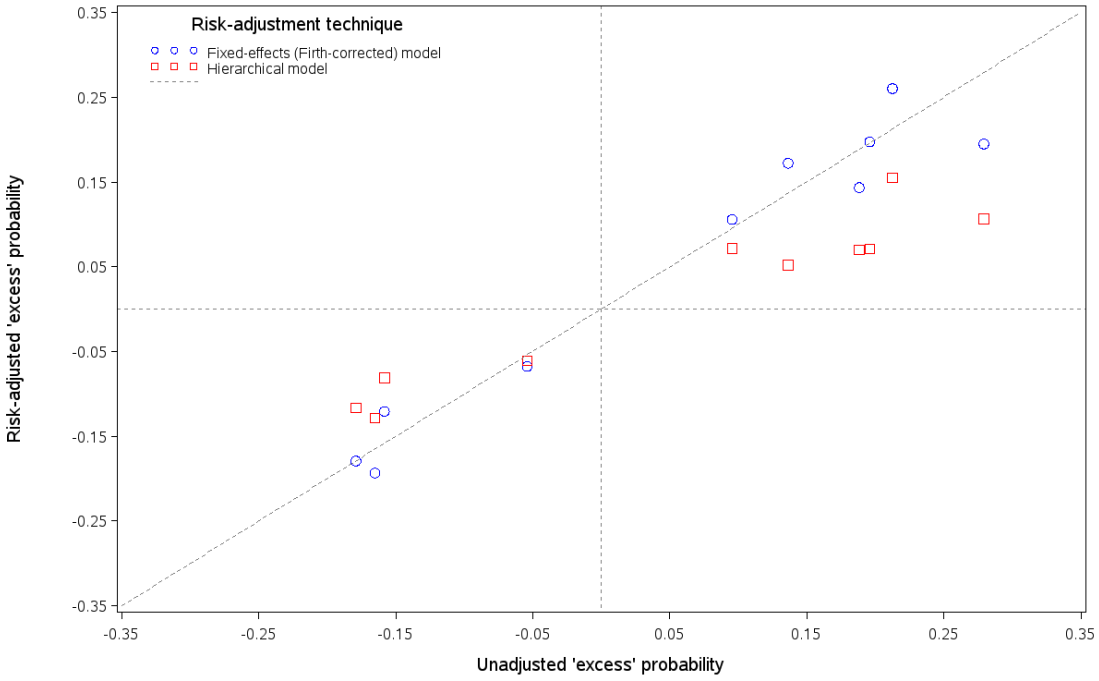
caterpillar plots (unadjusted and adjusted) in Figure 32 in Section 1, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

Table 99: Minimum, P25, P75, maximum and interquartile range (%) of the center-effects for QCI 1232b [%stoma1year] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-18	-16	20	28	36
Fixed-effects regression	-19	-12	20	26	32
Hierarchical regression	-13	-8	7	16	15

Figure 65 shows the relation between the adjusted and unadjusted center effects. From this we learn that the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects. Note that the shrinkage by the hierarchical model is much less pronounced than for e.g. QCI 1227 (Figure 63).

Figure 65: Scatter plot of adjusted center effects (from both fixed- and random effects outcome regression) versus unadjusted center effects for QCI 1232b [%stoma1year].



2.4.4 *Rate of patients with major leakage of the anastomosis after PME + SSO + reconstruction (new QCI 1233a, outcome)

2.4.4.1 Definition

N: Number of patients with major leakage of the anastomosis (requiring reoperation for leakage).

D: Number of patients treated with PME (high or low anterior resection with colorectal anastomsosis) and for whom it is reported whether there were postoperative complications or not.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

2.4.4.2 Description

There are 556 of the 3318 (17%) patients in the PROCARE database eligible for this QCI. Of these 556 patients, 32 (6%, or 5% unweighted) had a major leakage of the anastomosis after PME + SSO + reconstruction. The proportion of patients that achieved the QCI is shown in Table 40 (per size-grouped center) and Figure 33 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 27 of the 43 (merged) centers to 33% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

2.4.4.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors for were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus no prognostic factors for were identified for this QCI.

Empirical associations

We find no significant univariate associations between this QCI and prognostic factors.

2.4.4.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 34 in Section 1).

Unadjusted center effects range between -6% and 27% ‘excess’ probability of having a major leakage of the anastomosis after PME + SSO + reconstruction. Note that the ‘excess probabilities’ are automatically constrained between -6% and 94% (since 6%

of patients in the database achieved this QCI). The P25 and P75 are located at -3% respectively 4%, hence the interquartile range is 7%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of having a major leakage of the anastomosis after PME + SSO + reconstruction. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cStage and level of the tumor (high, mid or low) were considered.

A model with prognostic factors age, gender, tumor level, cStage and ASA score as main effects was retained. There is one significant interaction, between gender and the ASA score. The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 100 and interpreted as in Table 91.

Table 100: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1233a [%Leak_PME]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	0.98 [0.95, 1.01]	0.27	
Gender [ref. = Male]	Female	0.83 [0.21, 3.27]	0.80	
Tumor level [ref. = Low]	Mid	4.74 [0.61, 36.53]	0.09	
	High	2.02 [0.25, 16.38]		
	Missing	2.26 [0.19, 26.81]		
ASA score [ref. = I]	II	1.97 [0.67, 5.81]	0.02	
	III	6.07 [1.52, 24.17]		
	Missing	0.25 [0.02, 2.92]		
cStage [ref. = III]	0/I	0.82 [0.29, 2.31]	0.07	
	II	0.15 [0.03, 0.65]		
	IV	1.55 [0.60, 4.00]		
	X/Missing	0.98 [0.36, 2.66]		
Gender – ASA interaction [ref. = Male, I]	Female, II	0.21 [0.03, 1.32]	0.10	0.03
	Female, III	0.38 [0.05, 3.05]	0.36	
	Female, Missing	13.30 [0.68, 258.97]	0.09	

Adjusted center effects are estimated from a Firth-corrected logistic regression model and a hierarchical logistic regression model. Center effects are the center-specific 'excess' probabilities of having a major leakage of the anastomosis after PME + SSO + reconstruction, relative to the 'average' center.

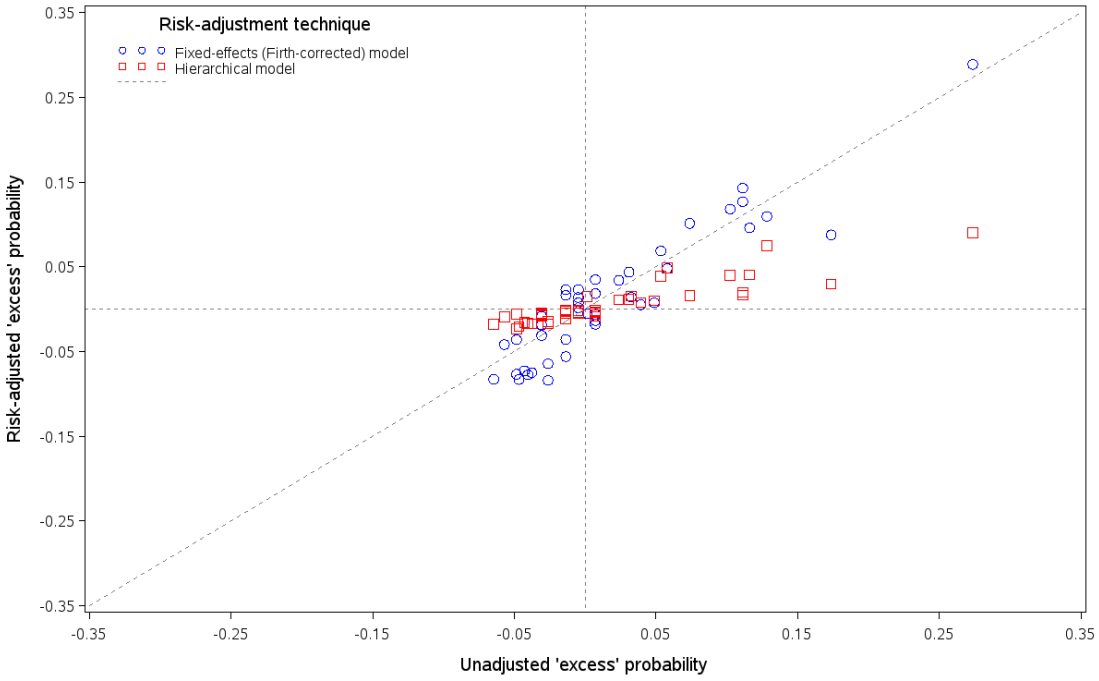
Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 34 in Section 1). Table 101 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and from the fixed-effects and hierarchical outcome regression. In the two caterpillar plots (unadjusted and adjusted) in Figure 34 in Section 1, we observe that there are no (merged) centers that perform significantly above P75.

Table 101: Minimum, P25, P75, maximum and interquartile range (%) of the center-effects for QCI 1233a [%Leak_PME] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-6	-3	4	27	7
Fixed-effects regression	-20	-8	8	41	16
Doubly-robust method	-9	-5	3	33	8

Figure 66 shows the relation between the adjusted and unadjusted center effects. From this we learn that the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects and that there is quite some shrinkage due to the hierarchical approach.

Figure 66: Scatter plot of adjusted center effects (from both fixed- and random effects outcome regression) versus unadjusted center effects for QCI 1233a [%Leak_PME].



2.4.5 *Rate of patients with major leakage of the anastomosis after TME + SSO + reconstruction (new QCI 1233b, outcome)

2.4.5.1 Definition

N: Number of patients with major leakage of the anastomosis (requiring reoperation for leakage)

D: Number of patients treated with TME (complete rectum resection (TME) + straight CAA, coloplasty, pouch, side-to-end CAA, total excision of colon and rectum with IPAA, or another specified type of reconstruction) and for whom it is reported whether there were postoperative complications or not.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

2.4.5.2 Description

There are 1592 of the 3318 (48%) patients in the PROCARE database eligible for this QCI. Of these 1592 patients, 91 (6% both weighted and unweighted) had a major leakage of the anastomosis after TME + SSO + reconstruction. The proportion of patients that achieved the QCI is shown in Table 41 (per size-grouped center) and Figure 35 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 16 of the 55 (merged) centers to 20% in 2 (merged) centers. The funnel plot does not point to systematic variation between the centers.

2.4.5.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors for were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the factors gender, age, ASA score, obesity and preoperative radio(chemo)therapy were identified as possible prognostic factors for this QCI. The former four will be considered in the model building procedure, but the latter is not a pre-treatment variable and will therefore not be considered in our risk-adjustment model.

Empirical associations

We find no significant univariate associations between this QCI and the prognostic factors.

2.4.5.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 36 in Section 1).

Unadjusted center effects range between -7% and 17% 'excess' probability of having a major leakage of the anastomosis after TME + SSO + reconstruction. Note that the 'excess probabilities' are automatically constrained between -6% and 94% (since 6% of patients in the database achieved this QCI). The P25 and P75 are located at -3% respectively 5%, hence the interquartile range is 8%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of patients having a major leakage of the anastomosis after TME + SSO + reconstruction. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cStage and level of the tumor (high, mid or low) were considered.

A model with prognostic factors age, gender, and ASA score as main effects was retained. There is one significant interaction, between age and the ASA score (*p*-value = 0.07). The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 102 and interpreted as in Table 91.

Table 102: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1233b [%Leak_TME]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	1.00 [0.97, 1.04]	0.80	
Gender [ref. = Male]	Female	0.94 [0.63, 1.40]	0.75	
ASA score [ref. = I]	II	0.80 [0.05, 12.70]	0.05	
	III	25.78 [0.74, 900.9]		
	Missing	0.002 [< 0.001, 2.10]		
Age – ASA interaction [ref. = (cont.), I]	II	1.00 [0.95, 1.04]	0.89	0.07
	III	0.96 [0.91, 1.01]	0.11	
	Missing	1.09 [0.99, 1.20]	0.08	

Adjusted center effects are estimated from a Firth-corrected logistic regression model and a hierarchical logistic regression model. Center effects are the center-specific 'excess' probabilities of having a major leakage of the anastomosis after TME + SSO + reconstruction, relative to the 'average' center.

Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 36 in Section 1). Table 103 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and from the fixed-effects and hierarchical outcome regression. In the two

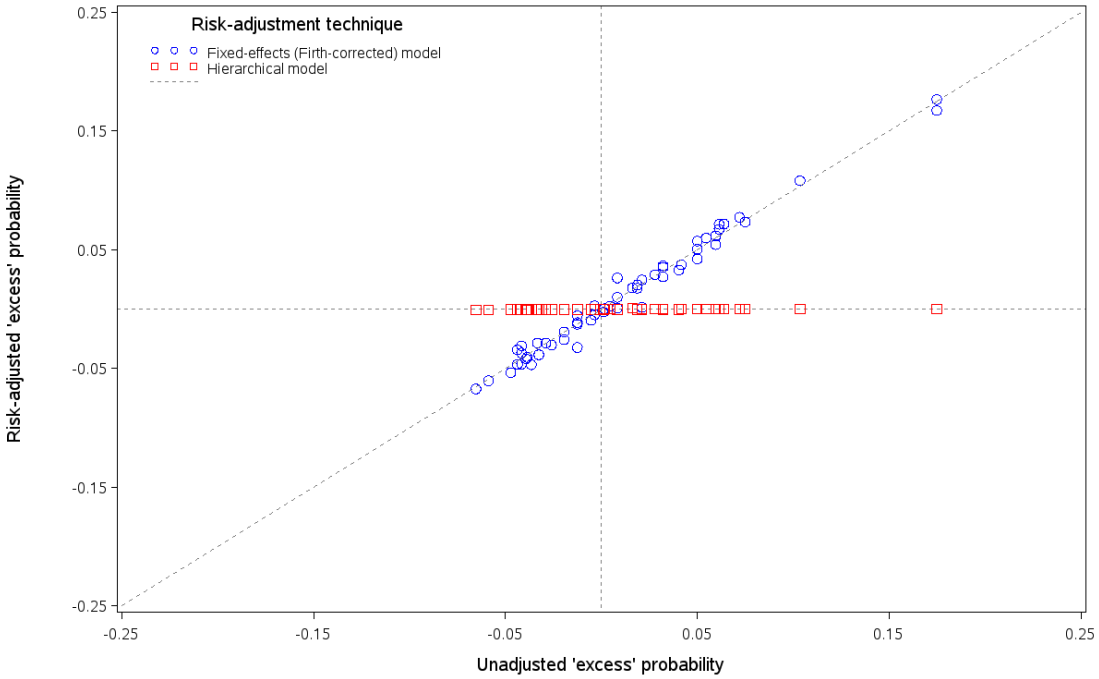
caterpillar plots (unadjusted and adjusted) in Figure 36 in Section 1, we observe one (merged) center performing significantly better than P25.

Table 103: Minimum, P25, P75, maximum and interquartile range (%) of the center-effects for QCI 1233b [%Leak_TME] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-6	-3	5	17	8
Fixed-effects regression	-7	-3	4	18	7
Hierarchical regression	-0.06	-0.01	0.01	0.1	0.02

Figure 67 shows the relation between the adjusted and unadjusted center effects. From this we learn the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects and that the shrinkage in the hierarchical regression model was quasi complete, all centers seem to have an 'excess' probability of 0. This strong shrinkage could be partly explained by the low percentage of events for this QCI and by a questionable fit of the hierarchical regression model.

Figure 67: Scatter plot of adjusted center effects (from both fixed- and random effects outcome regression) versus unadjusted center effects for QCI 1233b [%Leak_TME].



2.4.6 Inpatient or 30-day mortality (QCI 1234, outcome)

2.4.6.1 Definition

N: Number of patients in denominator who died within 30 days after surgery.

D: Number of patients treated with radical surgical resection and for whom it is known whether they died within 30 days after surgery and for whom the dates of surgery and survival or death are known.

Note that this definition was changed by PROCARE (deletion of the condition 'who died in hospital or within …' in both denominator and numerator) since the information about inpatient mortality was not reliable.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

2.4.6.2 Description

There are 2919 of the 3318 (88%) patients in the PROCARE database eligible for this QCI. Of these 2919 patients, 50 (2% both weighted and unweighted) died within 30 days after surgery. The proportion of patients that achieved the QCI is shown in Table 42 (per size-grouped center) and Figure 37 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 35 of the 68 (merged) centers to 13% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

2.4.6.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors for were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the factors age, ASA score, emergency surgery, ca excision and HCT were identified as possible prognostic factors for this QCI. The former three will be considered in the model building procedure, but the latter two are 1) not pre-treatment variables and 2) not found in the PROCARE database and will therefore not be considered in our risk-adjustment model.

Empirical associations

We find significant (*p*-value < 0.10) univariate associations between this QCI and seven prognostic factors, as shown in Table 104. The interpretation of the odds ratios is as described in Table 69.

Table 104: Odds ratio estimate [95% confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1234 [30d_mort]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	1.12 [1.08, 1.16]	<0.0001	<0.0001
Missing Age [ref. = Not missing]	Missing	0.02 [< 0.001, > 999.9]	1.00	
BMI	(continuous)	0.95 [0.87, 1.04]	0.26	0.03
Missing BMI [ref. = Not missing]	Missing	0.56 [0.06, 5.58]	0.62	
Gender [ref. = Male]	Female	0.55 [0.29, 1.05]	0.07	
ASA score [ref. = I]	II	6.74 [0.88, 51.95]	<0.0001	
	III-V	43.84 [5.98, 321.75]		
	Missing	12.15 [1.42, 104.4]		
cStage [ref. = III]	I	1.49 [0.53, 4.16]	0.003	
	II	2.01 [0.87, 4.68]		
	IV	3.84 [1.76, 8.37]		
	Missing / X	3.78 [1.66, 8.60]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	8.95 [3.62, 22.13]	<0.0001	
	Missing	0.92 [0.12, 6.74]		
cT4 [ref. = No]	Yes	1.19 [0.46, 3.04]	0.02	
	Missing	2.97 [1.41, 6.25]		

2.4.6.4 Estimation of unadjusted and case-mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 38 in Section 1).

Unadjusted center effects range between -2% and 12% 'excess' probability dying within 30 days after surgery. Note that the 'excess probabilities' are automatically constrained between -2% and 98% (since 2% of patients in the database achieved this QCI). The P25 and P75 are located at -2% respectively 2%, hence the interquartile range is 4%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of patients dying within 30 days after surgery. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cStage, level of the tumor (high, mid or low) and mode of surgery were considered.

A model with prognostic factors age, gender, ASA score and mode of surgery as main effects was retained. There is one significant interaction, between age and gender (*p*-value = 0.07). The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 105 and interpreted as in Table 91.

Table 105: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1234 [30d_mort].
For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	1.10 [1.06, 1.14]	<0.0001	<0.0001
Missing Age [ref. = Not missing]	Missing	> 999 [27.93, > 999]	0.0005	
Gender [ref. = Male]	Female	86.01 [1.05, > 999]	0.05	
ASA score [ref. = I]	II	3.48 [1.01, 12.05]	<0.0001	
	III-V	16.89 [4.75, 60.00]		
	Missing	3.99 [1.01, 15.85]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	5.89 [2.15, 16.15]	0.001	
	Missing	3.21 [0.66, 15.67]		
Age – Gender interaction [ref. = (cont.), Male]	Female	0.94 [0.88, 0.99]	0.02	0.06
Missing Age – Gender interaction [ref. = Not Missing, Male]	Missing, Female	0.03 [< 0.001, 13.42]	0.26	

Adjusted center effects are estimated from a Firth-corrected logistic regression model and a hierarchical logistic regression model. Center effects are the center-specific 'excess' probabilities of dying within 30 days after surgery, relative to the 'average' center.

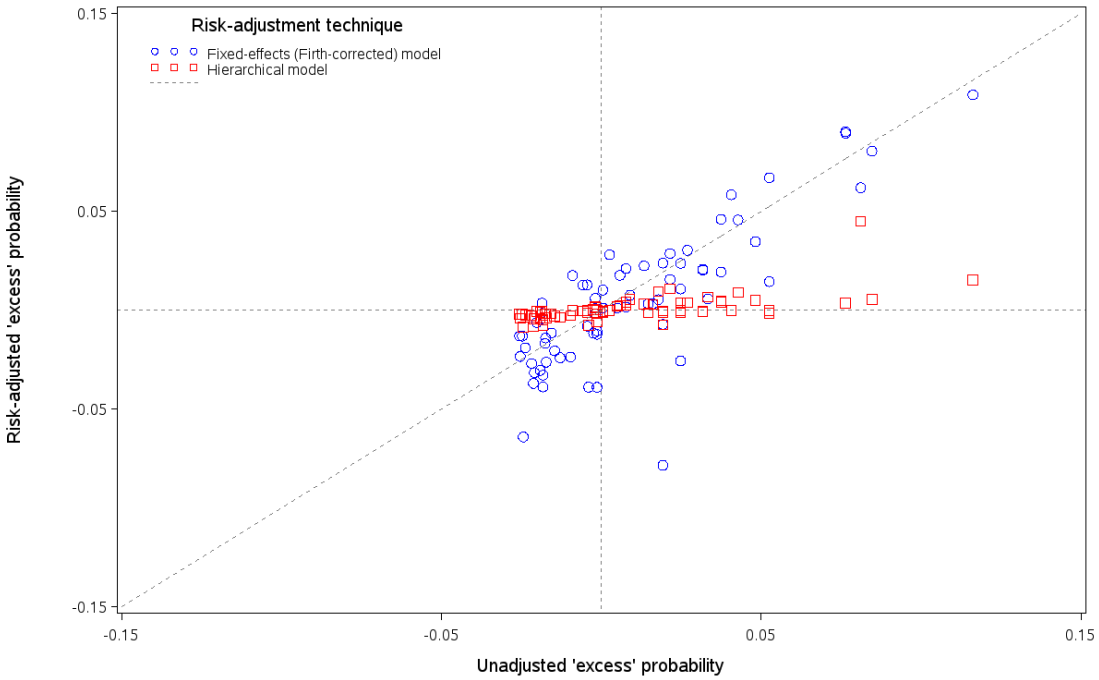
Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 38 in Section 1). Table 106 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and from the fixed-effects and hierarchical outcome regression. In the two caterpillar plots (unadjusted and adjusted) in Figure 38 in Section 1, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

Table 106: Minimum, P25, P75, maximum and interquartile range (%) of the center-effects (%) for QCI 1234 [30d_mort] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-2	-2	2	12	4
Fixed-effects regression	-8	-2	2	11	4
Hierarchical regression	-0.8	-0.2	0.3	5	0.5

Figure 68 shows the relation between the adjusted and unadjusted center effects. From this we learn the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects. Some longer deviations occur in centers that are evaluated lower in the adjusted analysis than in the unadjusted analysis. There is substantial shrinkage of center effects in the hierarchical regression model.

Figure 68: Scatter plot of adjusted center effects (from both fixed- and random effects outcome regression) versus unadjusted center effects for QCI 1234 [30d_mort].



2.4.7 *Postoperative major surgical morbidity with reintervention under narcosis after radical surgical resection (new QCI 1234b, outcome)

2.4.7.1 Definition

N: Number of patients in denominator who presented major surgical morbidity requiring reintervention under narcosis.

D: Number of patients treated with radical surgical resection and for whom postoperative data on morbidity/mortality are available.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

2.4.7.2 Description

There are 2913 of the 3318 (88%) patients in the PROCARE database eligible for this QCI. Of these 2913 patients, 167 (6% both weighted and unweighted) had a postoperative major surgical morbidity. The proportion of patients that achieved the QCI is shown in Table 43 (per size-grouped center) and Figure 39 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 18 of the 68 (merged) centers to 31% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

2.4.7.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors for were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the factors age, ASA score and emergency surgery were identified and will be considered as possible prognostic factors for this QCI.

Empirical associations

We find significant (*p*-value < 0.10) univariate associations between this QCI and two prognostic factors, as shown in Table 107. The interpretation of the odds ratios is as described in Table 69.

Table 107: Odds ratio estimate [95% confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1234b [%Major_morb].
For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
ASA score [ref. = I]	II	0.90 [0.61, 1.32]	0.05
	III-V	1.30 [0.84, 2.01]	
	Missing	0.50 [0.24, 1.03]	
Level [ref. = Low]	Mid	2.06 [1.42, 2.97]	0.001
	High	1.77 [1.12, 2.80]	
	Missing	0.94 [0.29, 3.10]	

2.4.7.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 40 in Section 1).

Unadjusted center effects range between -6% and 19% 'excess' probability having postoperative major surgical morbidity. Note that the 'excess probabilities' are automatically constrained between -6% and 94% (since 6% of patients in the database achieved this QCI). The P25 and P75 are located at -2% respectively 3%, hence the interquartile range is 5%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of patients having postoperative major surgical morbidity. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cStage, level of the tumor (high, mid or low) and mode of surgery were considered.

A model with prognostic factors age, gender, ASA score and tumor level as main effects was retained. There are two significant interactions, between age and ASA score (*p*-value = 0.0230) and gender and ASA score (*p*-value = 0.0867). The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic

factors in the multivariate risk-adjustment model are presented in Table 108 and interpreted as in Table 91.

Table 108: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1234b [%Major_morb]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	0.99 [0.96, 1.01]	0.32	
Gender [ref. = Male]	Female	1.02 [0.56, 1.86]	0.95	
Level [ref. = Low]	Mid	2.05 [1.45, 2.91]	0.0007	
	High	1.72 [1.10, 2.67]		
	Missing	1.09 [0.37, 3.22]		
ASA score [ref. = I]	II	0.55 [0.07, 4.53]	0.01	
	III-V	6.51 [0.43, 99.02]		
	Missing	< 0.001 [< 0.001, 0.11]		
Age – ASA score interaction [ref. = (cont.), I]	II	1.01 [0.98, 1.05]	0.50	0.02
	III-V	0.98 [0.94, 1.02]	0.32	
	Missing	1.12 [1.03, 1.22]	0.01	
Gender – ASA score interaction [ref. = Male, I]	Female, II	0.55 [0.25, 1.21]	0.14	0.09
	Female, III	1.27 [0.53, 3.01]	0.60	
	Female, Missing	2.00 [0.53, 7.54]	0.31	

The interaction between Age and the ASA score can be interpreted as follows:

- For a patient with ASA score I, an increase of 1 year in age *and otherwise the same characteristics with regard to gender and tumor level* corresponds to an increase in the odds of having postoperative major surgical morbidity with a factor 0.99 (95% CI [0.96, 1.01]).
- For a patient with missing ASA score, an increase of 1 year in age *and otherwise the same characteristics with regard to gender and tumor level* corresponds to an increase in the odds of having postoperative major surgical morbidity with a factor 1.11 (= 0.99 times 1.12), 95% confidence interval not provided.
- For a patient of e.g. age 50, the odds of having postoperative major surgical morbidity increase with a factor 2.47 (= 6.51 times exp(ln(0.98) times 50)) when changing from ASA score III-V to ASA score I whilst keeping *the characteristics for gender and tumor level fixed* (the 95% confidence interval is not provided).

Adjusted center effects are estimated from a Firth-corrected logistic regression model and a hierarchical logistic regression model. Center effects are the center-specific 'excess' probabilities of having postoperative major surgical morbidity, relative to the 'average' center.

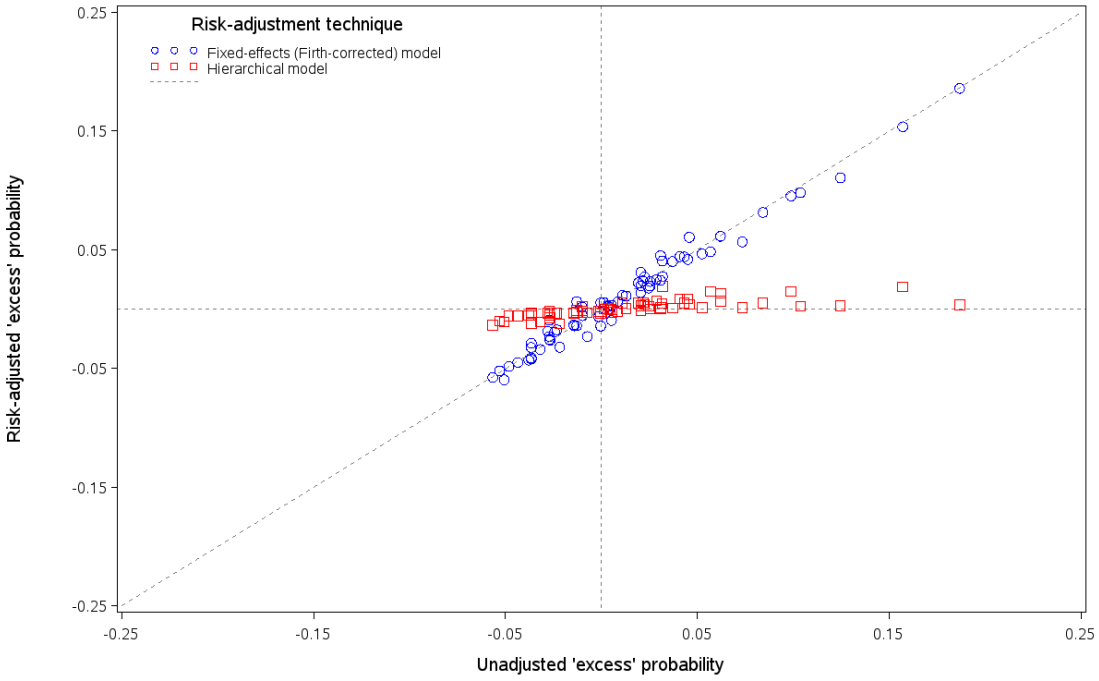
Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 40 in Section 1). Table 109 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and from the fixed-effects and hierarchical outcome regression. In the two caterpillar plots (unadjusted and adjusted) in Figure 40 in Section 1, we observe that there are two (merged) centers that perform significantly better than P25.

Table 109: Minimum, P25, P75, maximum and interquartile range (%) of the center-effects for QCI 1234b [%Major_morb] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-6	-2	3	19	5
Fixed-effects regression	-6	-2	4	19	6
Hierarchical regression	-1	-0.3	0.4	2	0.7

Figure 69 shows the relation between the adjusted and unadjusted center effects. From this we learn the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects and that there is substantial shrinkage in the hierarchical regression model.

Figure 69: Scatter plot of adjusted center effects (from both fixed- and random effects outcome regression) versus unadjusted center effects for QCI 1234b [%Major_morb].



2.4.8 *Rate of intra-operative rectal perforation (QCI 1235, outcome)

2.4.8.1 Definition

N: Number of patients in denominator for whom the surgeon and/or pathologist reported rectal perforation.

D: Number of patients treated with radical surgical resection and for whom perforation of the rectum (yes or no) is reported by either the surgeon or the pathologist.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

2.4.8.2 Description

There are 2900 of the 3318 (87%) patients in the PROCARE database eligible for this QCI. Of these 2900 patients, 220 (8% both weighted and unweighted) had an intra-operative rectal perforation. The proportion of patients that achieved the QCI is shown in Table 44 (per size-grouped center) and Figure 41 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 14 of the 68 (merged) centers to 33% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

2.4.8.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors for were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the factor age is identified and will be considered as possible prognostic factors for this QCI.

Empirical associations

We find significant (p-value < 0.10) univariate associations between this QCI and seven prognostic factors, as shown in Table 110. The interpretation of the odds ratios is as described in Table 69.

Table 110: Odds ratio estimate [95% confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1235 [%Perfor]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
ASA score [ref. = I]	II	1.21 [0.84, 1.75]	0.02
	III-V	1.50 [0.98, 2.29]	
	Missing	2.03 [1.28, 3.24]	
Level [ref. = Low]	Mid	0.65 [0.47, 0.88]	0.03
	High	0.67 [0.44, 1.00]	
	Missing	0.92 [0.42, 2.05]	
cStage [ref. = III]	0/I	0.76 [0.46, 1.26]	0.0002
	II	0.97 [0.65, 1.47]	
	IV	2.17 [1.50, 3.13]	
	Missing/X	1.02 [0.62, 1.67]	
Mode of surgery [ref. = Elective / Scheduled]	Urgent/Emergency	3.68 [1.85, 7.33]	0.001
	Missing	< 0.001 [< 0.001, > 999]	
Ventral tumor [ref. = No]	Yes	0.77 [0.56, 1.07]	0.06
	Missing	0.62 [0.40, 0.98]	
cT4 [ref. = No]	Yes	3.97 [2.85, 5.55]	< 0.0001
	Missing	1.22 [0.71, 2.12]	
Surgical technique [ref. = PME]	TME	1.60 [1.06, 2.41]	< 0.0001
	Missing	5.19 [2.57, 10.48]	

2.4.8.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 42 in Section 1).

Unadjusted center effects range between -7% and 27% 'excess' probability of having an intra-operative rectal perforation. Note that the 'excess probabilities' are automatically constrained between -8% and 92% (since 8% of patients in the database achieved this QCI). The P25 and P75 are located at -3% respectively 3%, hence the interquartile range is 6%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of patients having an intra-operative rectal perforation. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cStage and level of the tumor (high, mid or low) were considered.

A model with prognostic factors age, gender, ASA score, cStage and tumor level as main effects was retained. There are no significant interactions. The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 111 and interpreted as in Table 91.

Table 111: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1235 [%Perfor].
For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	0.99 [0.98, 1.00]	0.11	0.12
Age [ref. = Not missing]	Missing	0.08 [0.004, 1.51]	0.09	
Gender [ref. = Male]	Female	1.04 [0.79, 1.37]	0.79	
Level [ref. = Low]	Mid	0.61 [0.45, 0.83]	0.004	
	High	0.64 [0.42, 0.97]		
	Missing	1.44 [0.64, 3.24]		
ASA score [ref. = I]	II	1.34 [0.90, 2.00]	0.09	
	III-V	1.78 [1.09, 2.90]		
	Missing	1.66 [0.98, 2.80]		
cStage [ref. = III]	I	0.86 [0.53, 1.41]	0.0001	
	II	0.87 [0.58, 1.31]		
	IV	2.23 [1.53, 3.24]		
	Missing/X	0.99 [0.59, 1.65]		

Adjusted center effects are estimated from a Firth-corrected logistic regression model and a hierarchical logistic regression model. Center effects are the center-specific 'excess' probabilities of having an intra-operative rectal perforation, relative to the 'average' center.

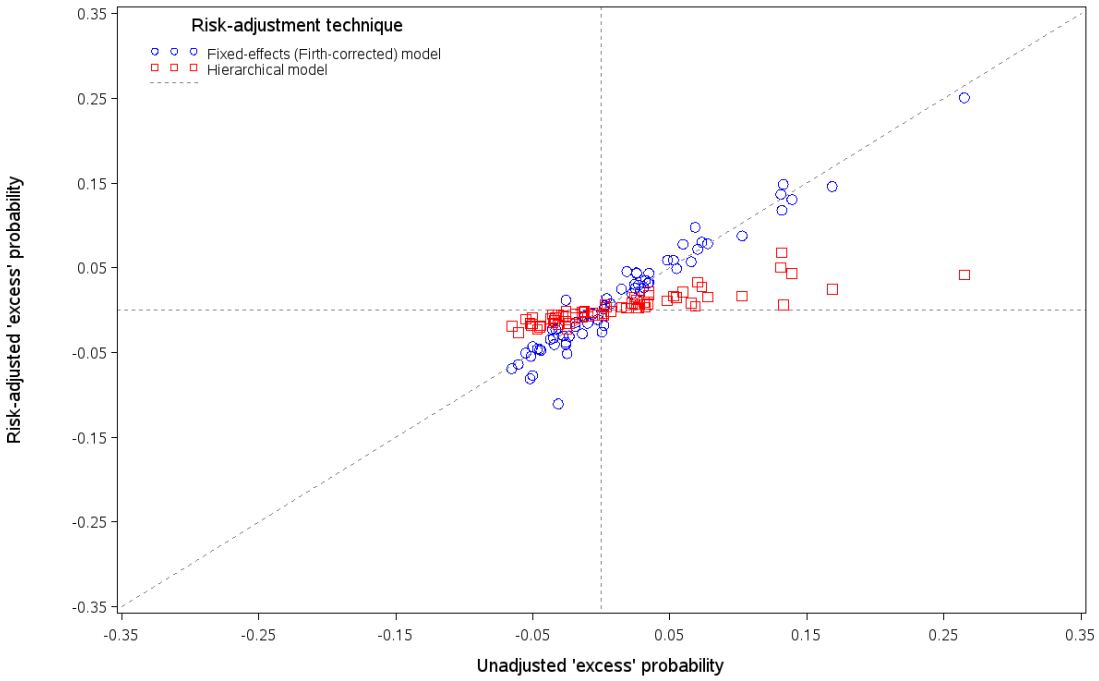
Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 42 in Section 1). Table 112 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and from the fixed-effects and hierarchical outcome regression. In the two caterpillar plots (unadjusted and adjusted) in Figure 42 in Section 1, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

Table 112: Minimum, P25, P75, maximum and interquartile range (%) of the center-effects for QCI 1235 [%Perfor] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-7	-3	3	27	6
Fixed-effects regression	-11	-3	5	25	8
Hierarchical regression	-3	-1	1	7	2

Figure 70 shows the relation between the adjusted and unadjusted center effects. From this we learn that the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects and that there is substantial shrinkage in the hierarchical regression model.

Figure 70: Scatter plot of adjusted center effects (from both fixed- and random effects outcome regression) versus unadjusted center effects for QCI 1235 [%Perfor].



2.4.9 *(y)p Distal margin involved (positive) after SSO or Hartmann for low rectal cancer (≤ 5 cm) (new QCI 1235b, outcome)

2.4.9.1 Definition

N: Number of patients in denominator for whom the (y)p distal margin is invaded.

D: Number of patients treated with Hartmann's procedure or SSO for rectal cancer in the lower third and for whom it is reported whether the (y)p distal margin is free or invaded.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

2.4.9.2 Description

There are 516 of the 3318 (16%) patients in the PROCARE database eligible for this QCI. Of these 516 patients, 9 (2% both weighted and unweighted) had an involved (y)p distal margin. The proportion of patients that achieved the QCI is shown in Table 45 (per size-grouped center) and Figure 43 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 21 of the 28 (merged) centers to 22% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

2.4.9.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors for were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus no prognostic factors for were identified for this QCI.

Empirical associations

We find no significant univariate associations between this QCI and the prognostic factors.

2.4.9.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 44 in Section 1).

Unadjusted center effects range between -4% and 20% 'excess' probability having an involved (y)p distal margin. Note that the 'excess probabilities' are automatically constrained between about -2% and 98% (since 2% of patients in the database achieved this QCI). The P25 and P75 are located at -2% respectively 3%, hence the interquartile range is 5%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of patients having an involved (y)p distal margin. In this, the prognostic factors gender, age, BMI, ASA co-morbidity score, cStage and level of the tumor (high, mid or low) were considered.

A model with prognostic factors age, gender and ASA score was retained. There are no significant interactions. The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 113.

Table 113: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1235b [%Pos_Dist_margin]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age	(continuous)	1.03 [0.98, 1.07]	0.29
Gender [ref. = Male]	Female	1.74 [0.66, 4.61]	0.27
ASA score [ref. = I]	II	0.06 [0.01, 0.29]	0.003
	III-V	0.18 [0.03, 0.93]	
	Missing	0.18 [0.02, 1.53]	

Adjusted center effects are estimated from a Firth-corrected logistic regression model and a hierarchical logistic regression. Center effects are the center-specific 'excess' probabilities of having an involved (y)p distal margin, relative to the 'average' center.

In this case, the optimization algorithm of the hierarchical model did not converge, hence no center effects could be estimated for this method.

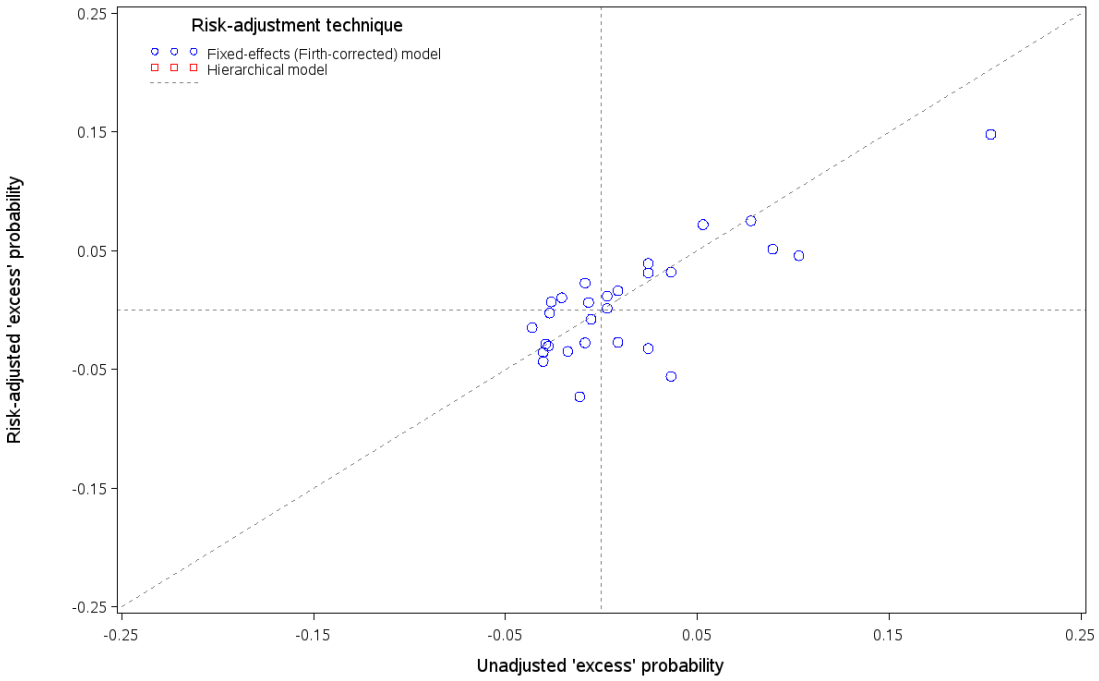
Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 44 in Section 1). Table 114 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and from the fixed-effects outcome regression. In the two caterpillar plots (unadjusted and adjusted) in Figure 44 in Section 1, we observe that there are no (merged) centers that perform significantly below P25 or above P75.

Table 114: Minimum, P25, P75, maximum and interquartile range (%) of the center-effects for QCI 1235b [%Pos_Dist_margin] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-4	-2	3	20	5
Fixed-effects regression	-7	-3	3	15	6

Figure 71 shows the relation between the adjusted and unadjusted center effects. From this we learn the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted effects.

Figure 71: Scatter plot of adjusted center effects (from fixed-effects outcome regression) versus unadjusted center effects for QCI 1235b [%Pos_Dist_margin].



2.4.10 *Mesorectal (y)pCRM positivity after radical surgical resection (new QCI 1235c, outcome)

2.4.10.1 Definition

N: Number of patients in denominator for whom the mesorectal (y)pCRM ≤ 1 mm.

D: Number of patients treated with radical surgical resection and for whom the mesorectal (y)pCRM is known.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

Note that there is also a version of this QCI for patients with 1) high RC, 2) mid RC and 3) low RC. In this report we only focus on the global version.

2.4.10.2 Description

There are 1932 of the 3318 (58%) patients in the PROCARE database eligible for this QCI. Of these 1932 patients, 361 (19%, or 18% unweighted) had mesorectal (y)pCRM positivity after radical surgical resection. The proportion of patients that achieved the QCI is shown in Table 46 (per size-grouped center) and Figure 45 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 6 of the 61 (merged) centers to 44% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

2.4.10.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus the prognostic factors ventral tumor, Ccrm positivity (< 5mm), (y)pStage, (y)pT and (y)pN were identified as possible prognostic factors for this QCI. The former two will be considered in the model building step, but the other three are not pre-treatment variables and hence not eligible for entering our risk adjustment model.

Empirical associations

We find significant (*p*-value < 0.10) univariate associations between this QCI and three prognostic factors, as shown in Table 115. The interpretation of the odds ratios is as described in Table 69.

Table 115: Odds ratio estimate [95% confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1235c [%Pos_CRM].
For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
cStage [ref. = III]	0/I	0.27 [0.15, 0.47]	< 0.0001
	II	0.85 [0.60, 1.19]	
	IV	2.11 [1.53, 2.90]	
	Missing/X	1.49 [1.01, 2.21]	
Mode of surgery [ref. = Elective / Scheduled]	Urgent/Emergency	2.55 [1.20, 5.41]	0.04
	Missing	0.69 [0.27, 1.78]	
cT4 [ref. = No]	Yes	3.74 [2.73, 5.15]	< 0.0001
	Missing	1.56 [1.01, 2.43]	

2.4.10.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 46 in Section 1).

Unadjusted center effects range between -15% and 26% 'excess' probability of having mesorectal (y)pCRM positivity after radical surgical resection. Note that the 'excess probabilities' are automatically constrained between -19% and 81% (since 19% of patients in the database achieved this QCI). The P25 and P75 are located at -6% respectively 9%, hence the interquartile range is 15%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of patients having mesorectal (y)pCRM positivity after radical surgical resection. In this, the prognostic factors gender, age,

BMI, ASA co-morbidity score, cT4, level of the tumor (high, mid or low), ventral tumor and cCRM positivity were considered.

A model with prognostic factors age, gender and cT4 as main effects was retained. There are no significant interactions. The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 116.

Table 116: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1235c [%Pos_CRM]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age	(continuous)	1.00 [0.99, 1.01]	0.62	0.61
Age [ref. = Not missing]	Missing	2.68 [0.38, 19.11]	0.33	
Gender [ref. = Male]	Female	1.02 [0.80, 1.30]	0.90	
cT4 [ref. = No]	Yes	4.03 [2.86, 5.69]	< 0.0001	
	Missing	1.82 [1.12, 2.94]		

Adjusted center effects are estimated from a Firth-corrected logistic regression model and a hierarchical logistic regression model. Center effects are the center-specific 'excess' probabilities of having mesorectal (y)pCRM positivity after radical surgical resection, relative to the 'average' center.

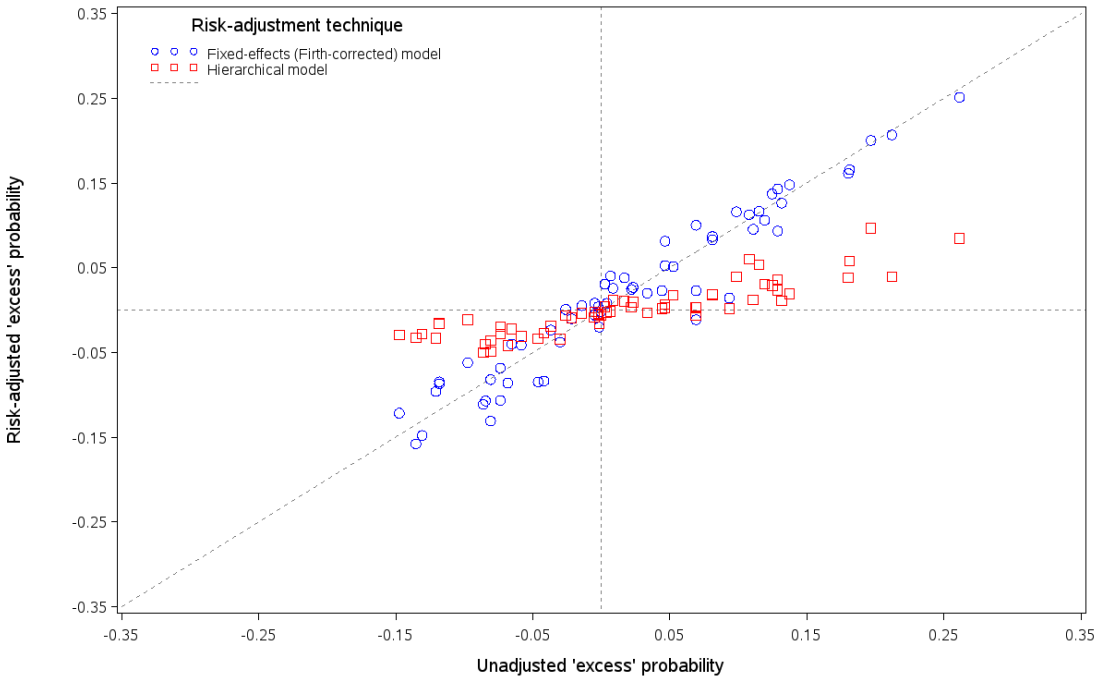
Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 46 in Section 1). Table 117 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and from the fixed-effects and hierarchical outcome regression. In the two caterpillar plots (unadjusted and adjusted) in Figure 46 in Section 1, we observe that there are no (merged) centers that perform significantly above P75.

Table 117: Minimum, P25, P75, maximum and interquartile range of the center-effects (%) for QCI 1235c [%Pos_CRM] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-15	-6	9	26	15
Fixed-effects regression	-16	-6	9	25	15
Hierarchical regression	-5	-2	2	10	4

Figure 72 shows the relation between the adjusted and unadjusted center effects. From this we learn the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects and that there is a degree of shrinkage in the center effects obtained from the hierarchical regression.

Figure 72: Scatter plot of adjusted center effects (from fixed-effects outcome regression and hierarchical regression) versus unadjusted center effects for QCI 1235c [%Pos_CRM].



2.5 QUALITY INDICATORS RELATED TO ADJUVANT TREATMENT

It should be noted that there is generally very few information available about adjuvant treatment of patients in the PROCARE database. This will be clear from the number of eligible patients in the QCIs below.

The main reason for the lack of information is that postoperative chemotherapy and/or radiotherapy reports are rarely sent to the BCR. If the report was sent this implies that there has been adjuvant therapy, hence performing statistical analyses on these data will always be biased.

2.5.1 Proportion of (y)pStage III patients with R0 resection that received adjuvant chemotherapy within 3 months after surgery (QCI 1241, process)

2.5.1.1 Definition

N: Number of patients in denominator receiving adjuvant chemotherapy within 3 months after surgery.

D: Number of patients treated with R0 radical surgical resection for (y)pStage III and for whom the start date of adjuvant chemotherapy is known.

Note that the condition ‘for whom the start date of adjuvant chemotherapy is known’ can currently not be assessed reliably in the PROCARE database because of the low quality of treatment data.

2.5.1.2 Description

There are 28 (or 1%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 24 (86%, or 87% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 47 (per size-grouped center) in Section 1.

2.5.1.3 Univariate associations with prognostic factors

Despite the very small number of eligible patients, we find a significant univariate association between this QCI and the prognostic factor pre-operative incontinence, as shown in Table 118. The interpretation of the odds ratio is as described in Table 69. Note that in the small subset of eligible patients, preoperative incontinence was never missing (hence only the 'Yes' level).

Table 118: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1241 [%Adj-Chemo<3m]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Preoper. incontinence [ref. = No]	Yes	0.09 [0.01, 1.04]	0.05

2.5.1.4 Estimation of unadjusted center effects

Given the very limited amount of information, it is not meaningful to estimate center effects.

2.5.2 Proportion of pStage II-III patients with R0 resection that received adjuvant radiotherapy or chemoradiotherapy within 6 months after surgery (QCI 1242, process)

2.5.2.1 Definition

N: Number of patients in denominator receiving adjuvant radio(chemo)therapy within 6 months after surgery.

D: Number of patients treated with R0 radical surgical resection for (y)pStage II or III without neoadjuvant treatment and for whom the start date of adjuvant chemo and the surgery date are known.

Note that the condition 'without neoadjuvant treatment' can currently not be assessed reliably in the PROCARE database because of the low quality of treatment data.

2.5.2.2 Description

There are 46 (or 1%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 45 (98%, or 99% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 48 (per size-grouped center) in Section 1.

2.5.2.3 Univariate associations with prognostic factors

Given the very small number of eligible patients, we find no significant univariate association between this QCI and any of the candidate prognostic factors.

2.5.2.4 Estimation of unadjusted center effects

Given the amount of information, it is not meaningful to estimate center effects.

2.5.3 Proportion of (y)pStage II-III patients with R0 resection that started adjuvant chemotherapy for (y)pStage II or III within 12 weeks after surgery (QCI 1243, process)

2.5.3.1 Definition

N: Number of patients in denominator receiving adjuvant chemotherapy within 3 months after surgery

D: Number of patients treated with R0 radical surgical resection for (y)pStage II or III and for whom the start date of adjuvant chemotherapy is known.

2.5.3.2 Description

There are 58 (or 2%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 54 (93%, both weighted and unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 49 (per size-grouped center) in Section 1.

2.5.3.3 Univariate associations with prognostic factors

Given the very small number of eligible patients, we find no significant univariate association between this QCI and any of the candidate prognostic factors.

2.5.3.4 Estimation of unadjusted center effects

Given the amount of information, it is not meaningful to estimate center effects.

2.5.4 Proportion of (y)pStage II-III patients with R0 resection treated with adjuvant chemo(radio)therapy, that received 5-FU based chemotherapy (QCI 1244, process)

2.5.4.1 Definition

N: Number of patients in denominator receiving 5-fluorouracil based adjuvant chemotherapy

D: Number of patients who received adjuvant (radio)chemotherapy within 6 months after R0 radical surgical resection for (y)pStage II or III and for whom the type of adjuvant chemotherapy is known.

Note that the condition ‘patients who received adjuvant (radio)chemotherapy’ can currently not be assessed reliably in the PROCARE database because of the low quality of treatment data.

2.5.4.2 Description

There are 57 (or 2%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 54 (95%, or 97% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 50 (per size-grouped center) in Section 1.

2.5.4.3 Univariate associations with prognostic factors

Given the very small number of eligible patients, we find no significant univariate association between this QCI and any of the candidate prognostic factors.

2.5.4.4 Estimation of unadjusted center effects

Given the amount of information, it is not meaningful to estimate center effects.

2.5.5 *Rate of acute grade 4 chemotherapy-related complications (QCI 1245, outcome)

2.5.5.1 Definition

N: Number of patients in denominator that presented acute grade 4 complications during or within 4 weeks after completion of adjuvant chemo(radio)therapy

D: Number of patients treated with adjuvant chemotherapy and for whom follow-up data (at least until 1 year) are available.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

Note that the condition 'patients treated with adjuvant chemotherapy' can currently not be assessed reliably in the PROCARE database because of the low quality of treatment data.

2.5.5.2 Description

There are 128 patients of the 3318 (4%) patients in the PROCARE database eligible for this QCI. Of these 128 eligible patients, 10 (8%, or unweighted 5%) presented acute grade 4 complications during or within 4 weeks after completion of adjuvant chemo(radio)therapy. The proportion of patients that achieved the QCI is shown in Table 51 (per size-grouped center) and Figure 47 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 6 of the 11 (merged) centers to 20% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

2.5.5.3 Identification of relevant prognostic factors

Prognostic factors identified in the literature review of Appendix 2

In Appendix 2 no prognostic factors for were identified for this QCI.

Prognostic factors identified in the PROCARE consensus on risk/confounding factors per QCI

In the PROCARE consensus no prognostic factors were identified for this QCI.

Empirical associations

We find a borderline significant (*p*-value = 0.09) univariate associations between this QCI and gender, as shown in Table 119. The interpretation of the odds ratios is as described in Table 69.

Table 119: Odds ratio [95% Wald confidence interval] estimate and corresponding p-value from the univariate logistic regression models for QCI 1245 [%grade4_Tox_Prostop_CT].

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Gender [ref. = Male]	Female	3.16 [0.84, 11.85]	0.09

2.5.5.4 Estimation of unadjusted and case mix adjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 48 in Section 1).

Unadjusted center effects range between -4% and 15% 'excess' probability of acute grade 4 complications during or within 4 weeks after completion of adjuvant chemo(radio)therapy. Note that the 'excess probabilities' are automatically constrained between -8% and 98% (since 8% of patients in the database achieved this QCI). The P25 and P75 are located at -3% respectively 3%, hence the interquartile range is 6%.

A model building procedure was performed to identify joint associations between prognostic factors and the proportion of acute grade 4 complications during or within 4 weeks after completion of adjuvant chemo(radio)therapy. In this, the prognostic factors gender, age, BMI, cStage, ASA co-morbidity score and level of the tumor (high, mid or low) were considered.

A model with the (non-significant) minimal set of prognostic factors, age and gender, was retained. The odds ratios (with corresponding 95% confidence interval and *p*-value) for the prognostic factors in the multivariate risk-adjustment model are presented in Table 120 and interpreted as in Table 91.

Table 120: Odds ratio [95% confidence interval] estimate and corresponding p-value from the final multivariate (Firth-corrected) logistic regression model for QCI 1245 [%grade4_Tox_Prostop_CT]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
Age	(continuous)	0.99 [0.94, 1.05]	0.83
Gender [ref. = Male]	Female	1.00 [0.63, 6.35]	0.24

Adjusted center effects are estimated from a fixed effects outcome regression (i.e. from a Firth-corrected logistic regression model) and a hierarchical logistic regression model. Unfortunately, the hierarchial logistic regression model could not be fit reliably on this few number of observations and events.

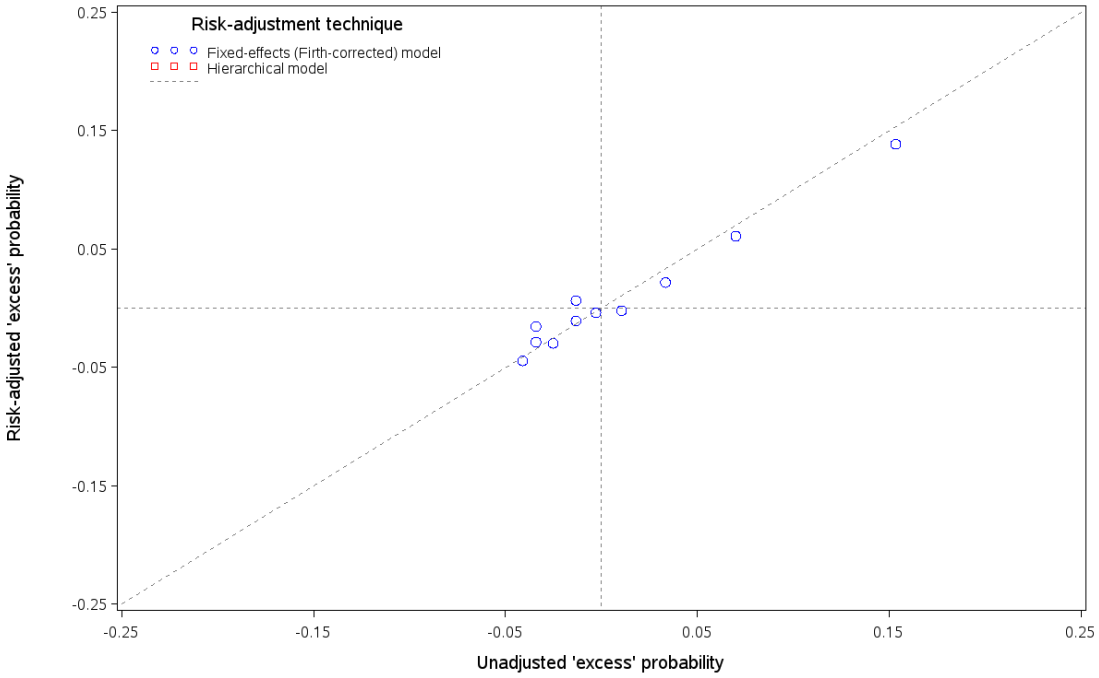
Adjusted center effects (as obtained from the fixed-effects outcome regression) are shown in a caterpillar plot (Figure 48 in Section 1). Table 121 contains a basic summary of the distribution of the center effects as obtained from the unadjusted analysis and the fixed-effects regression.

Table 121: Minimum, P25, P75, maximum and interquartile range of the center-effects for QCI 1245 [%grade4_Tox_Prostop_CT] as estimated by different methods.

Method	Min	P25	P75	Max	IQR
Unadjusted	-4	-3	3	15	6
Fixed-effects regression	-4	-3	2	14	5

Figure 73 shows the relation between the adjusted and unadjusted center effects. From this we learn that the center effects obtained from the fixed effects adjustment model stay generally close to the unadjusted center effects.

Figure 73: Scatter plot of adjusted center effects (from fixed-effects regression) versus unadjusted center effects for QCI 1245 [%grade4_Tox_Prostop_CT].



2.6 QUALITY INDICATORS RELATED TO PALLIATIVE TREATMENT

2.6.1 Rate of cStage IV patients receiving chemotherapy (QCI 1251, process)

2.6.1.1 Definition

N: Number of patients in denominator that received chemotherapy

D: Number of patients with cStage IV and for whom it is known whether they received chemotherapy or not.

2.6.1.2 Description

In view of the limited number of adequate and updated follow-up date, no valuable analysis can be performed for this QCI.

2.7 QUALITY INDICATORS RELATED TO FOLLOW-UP

2.7.1 Rate of curatively treated patients that received a colonoscopy within 1 year after resection (QCI 1261, process)

2.7.1.1 Definition

N: Number of patients in denominator that received a colonoscopy.

D: Number of patients treated with curative resection for c(p)Stage I-III and for whom follow-up data (at least until 2 years) are available.

2.7.1.2 Description

This QCI cannot be computed reliably yet, but will be in the future. It is not further considered in the report.

2.7.2 *Late grade 4 complications of radiotherapy or chemoradiation (QCI 1263, outcome)

2.7.2.1 Definition

N: Number of patients in the denominator that presented late grade 4 complications after completion of (neo)adjuvant chemo(radio)therapy (excluding early toxicity).

D: Number of patients treated with neoadjuvant or adjuvant radio(chemo)therapy and for whom follow-up data (at least until 1 year) are available.

Note that – contrary to most other QCIs - fulfilling the QCI is not a positive event.

Note that the BCR did not determine the denominator of this QCI in the same way as the denominator for QCI 1245 (Rate of acute grade 4 chemotherapy-related complications), too few patients were discarded from the denominator for the current QCI.

Either way the condition 'patients treated with neoadjuvant or adjuvant radio(chemo)therapy' can currently not be assessed reliably in the PROCARE database because of the low quality of treatment data.

2.7.2.2 Description

There are 1890 patients of the 3318 (4%) patients in the PROCARE database eligible for this QCI. Of these 1890 eligible patients, 4 (0%, both weighted and unweighted) presented late grade 4 complications of radiotherapy or chemoradiation. The proportion of patients that achieved the QCI is shown in Table 52 (per size-grouped center) and Figure 49 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in 58 of the 62 (merged) centers to 4% in one (merged) center. The funnel plot does not point to systematic variation between the centers.

Because there are only 4 patients who presented late grade 4 complications after completion of (neo)adjuvant chemo(radio)therapy, each in a different center, this QCI is not further usable for evaluating the quality of rectum cancer care on center level. On a patient level we can state that all centers perform very well for this QCI.

2.8 QUALITY INDICATORS RELATED TO HISTOPATHOLOGIC EXAMINATION

2.8.1 Use of the pathology report sheet (QCI 1271, process)

2.8.1.1 Definition

N: Number of patients in denominator for whom a pathology report sheet was completed.

D: Number of patients treated with (local or radical) resection and for whom date of resection is later than or equal to the January 1st, 2007.

2.8.1.2 Description

There are 1980 (or 60%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 1938 (98%, both weighted and unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 53 (per size-grouped

center) and Figure 50 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 75% in one of the 57 (merged) centers to 100% in forty-two (merged) centers. The funnel plot points to systematic variation between the centers.

2.8.1.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and two prognostic factors, as shown in Table 122. The interpretation of the odds ratios is as described in Table 69. Note that the odds of using the pathology report sheet are higher for patients with cStage II and lower for patients with cStage I or IV (compared to patients with cStage III).

Table 122: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1271 [%Path_Rep_Use]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value
cStage [ref. = III]	I	0.73 [0.31, 1.73]	0.09
	II	3.09 [0.72, 13.23]	
	IV	0.86 [0.32, 2.31]	
	Missing / X	0.39 [0.17, 0.95]	
cT4 [ref. = No]	Yes	0.46 [0.20, 1.07]	0.003
	Missing	0.23 [0.09, 0.57]	

2.8.1.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 50 in Section 1). These center effects range between -23% and 2% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -98% and 2% (since 98% of patients in the database achieved this QCI). The P25 and P75 are located at -2% resp. 2%, hence the interquartile range is 4%. In the caterpillar plot, we observe that two (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25.

2.8.2 Quality of TME assessed according to Quirke and mentioned in the pathology report (QCI 1272, process)

2.8.2.1 Definition

N: Number of patients for whom the external surface of TME was reported in the pathology report sheet.

D: Number of patients treated with TME as indicated by the surgeon after the January 1st, 2007.

2.8.2.2 Description

There are 1572 (or 47%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 1074 (68%, or 64% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 54 (per size-grouped center) and Figure 51 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in two of the 55 (merged) centers to 100% in four (merged) centers. The funnel plot points to systematic variation between the centers.

2.8.2.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and six prognostic factors, as shown in Table 123. The interpretation of the odds ratios is as described in Table 69.

Table 123: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1272 [%TME_Qual_Rep]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
BMI	(continuous)	1.02 [0.99, 1.05]	0.24	0.003
Missing BMI [ref. = Not missing]	Missing	1.03 [0.49, 2.18]	0.93	
ASA score [ref. = I]	II	1.30 [1.00, 1.70]	0.01	
	III-V	0.94 [0.69, 1.29]		
	Missing	0.75 [0.49, 1.15]		
cStage [ref. = III]	I	0.77 [0.54, 1.08]	0.0008	
	II	0.55 [0.41, 0.74]		
	IV	0.65 [0.46, 0.92]		
	Missing / X	0.72 [0.45, 1.17]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	0.23 [0.09, 0.61]	0.008	
	Missing	1.65 [0.61, 4.47]		
cCRM positive [ref. = No]	Yes	1.21 [0.73, 2.02]	<0.0001	
	Missing	0.59 [0.38, 0.93]		
cT4 [ref. = No]	Yes	0.86 [0.61, 1.21]	0.04	
	Missing	0.47 [0.25, 0.86]		

2.8.2.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 51 in Section 1). These center effects range between -63% and 29% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -68% and 32% (since 68% of patients in the database achieved this QCI). The P25 and P75 are located at -21% resp. 16%, hence the interquartile range is 37%. In the caterpillar plot, we observe that three (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25. We also observe that two

(merged) centers perform significantly above P75, i.e. the lower bounds of their confidence intervals are higher than P75.

2.8.3 Distal tumor-free margin mentioned in the pathology report (QCI 1273, process)

2.8.3.1 Definition

N: Number of patients in denominator for whom the length of the distal free tumor free margin was reported in the pathology report.

D: Number of patients treated with SSO or Hartmann's procedure.

Note that patients with (y)pT0 and (y)pTis are excluded for analysis.

2.8.3.2 Description

There are 2051 (or 62%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 1763 (86%, or 83% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 55 (per size-grouped center) and Figure 52 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in two of the 64 (merged) centers to 100% in thirteen (merged) centers. The funnel plot points to systematic variation between the centers.

2.8.3.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and ten prognostic factors, as shown in Table 124. The interpretation of the odds ratios is as described in Table 69.

Table 124: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1273 [%Dist_Margin_Rep]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
BMI	(continuous)	0.61 [0.25, 1.49]	0.27	<0.0001
Missing BMI [ref. = Not missing]	Missing	1.00 [0.97, 1.04]	0.84	
Tumor level [ref. = Low]	Mid	0.78 [0.56, 1.07]	0.0004	
	High	0.69 [0.48, 0.99]		
	Missing	0.27 [0.14, 0.49]		
ASA score [ref. = I]	II	1.11 [0.81, 1.53]	0.004	
	III-V	0.81 [0.56, 1.17]		
	Missing	0.55 [0.36, 0.85]		
cStage [ref. = III]	I	0.65 [0.44, 0.94]	<0.0001	
	II	0.77 [0.53, 1.12]		
	IV	0.74 [0.49, 1.10]		
	Missing / X	0.40 [0.28, 0.58]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	0.54 [0.26, 1.10]	<0.0001	
	Missing	0.27 [0.14, 0.51]		
Ventral tumor [ref. = No]	Yes	1.25 [0.90, 1.73]	<0.0001	
	Missing	0.55 [0.40, 0.75]		
cCRM positive [ref. = No]	Yes	2.15 [1.10, 4.20]	0.006	
	Missing	1.01 [0.60, 1.70]		
cT4 [ref. = No]	Yes	0.86 [0.54, 1.38]	0.09	
	Missing	0.64 [0.43, 0.96]		
Preoper. incontinence [ref. = No]	Yes	0.83 [0.57, 1.21]	<0.0001	
	Missing	0.25 [0.16, 0.40]		
Surgical technique [ref. = PME]	TME	1.63 [1.24, 2.13]	<0.0001	
	Missing	0.48 [0.21, 1.09]		

2.8.3.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 52 in Section 1). These center effects range between -82% and 12% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -86% and 14% (since 86% of patients in the database achieved this QCI). The P25 and P75 are located at -10% resp. 7%, hence the interquartile range is 17%. In the caterpillar plot, we observe that four (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25.

2.8.4 Distal margin involvement mentioned after SSO or Hartmann (new QCI 1273b, process)

2.8.4.1 Definition

N: Number of patients in denominator for whom it was reported whether the distal resection margin was invaded or not.

D: Number of patients treated with Hartmann's procedure or SSO with reconstruction and for whom a pathology report sheet was completed.

Note that patients with (y)pT0 and (y)pTis are excluded for analysis.

2.8.4.2 Description

There are 2034 (or 61%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 1860 (91%, or 88% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 56 (per size-grouped center) and Figure 53 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in two of the 64 (merged) centers to 100% in 18 (merged) centers. The funnel plot points to systematic variation between the centers.

2.8.4.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and seven prognostic factors, as shown in Table 125. The interpretation of the odds ratios is as described in Table 69.

Table 125: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1273b [%Dist_Margin_Pos_Rep]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
BMI	(continuous)	1.01 [0.97, 1.06]	0.62	0.002
Missing BMI [ref. = Not missing]	Missing	0.75 [0.24, 2.37]	0.63	
Tumor level [ref. = Low]	Mid	0.61 [0.40, 0.92]	0.0008	
	High	0.60 [0.37, 0.96]		
	Missing	0.22 [0.11, 0.47]		
ASA score [ref. = I]	II	1.67 [1.13, 2.45]	0.002	
	III-V	1.24 [0.78, 1.95]		
	Missing	0.70 [0.43, 1.14]		
cStage [ref. = III]	I	0.70 [0.43, 1.12]	0.02	
	II	0.66 [0.42, 1.03]		
	IV	0.75 [0.45, 1.24]		
	Missing / X	0.46 [0.29, 0.73]		
Ventral tumor [ref. = No]	Yes	1.20 [0.80, 1.80]	0.004	
	Missing	0.58 [0.39, 0.85]		
Preoper. incontinence [ref. = No]	Yes	0.79 [0.50, 1.26]	<0.0001	
	Missing	0.30 [0.17, 0.51]		
Surgical technique [ref. = PME]	TME	1.97 [1.42, 2.73]	<0.0001	
	Missing	0.51 [0.20, 1.30]		

2.8.4.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 53 in Section 1). These center effects range between -86% and 8% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -91% and 9% (since 91% of patients in the database achieved this QCI). The P25 and P75 are located at -9% resp. 5%, hence the interquartile range is 14%. In the caterpillar plot, we

observe that two (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25.

2.8.5 Number of lymph nodes examined (QCI 1274, process)

2.8.5.1 Definition

The number of lymph nodes examined.

D: All patients treated with radical surgical resection for whom the number of examined lymph nodes is mentioned in the pathology report.

2.8.5.2 Description

Of the 3318 patients, 2714 (82%) are eligible for the denominator of this QCI. Of the 604 patients who are not eligible, 594 had either a missing surgical resection status or missing number of lymph nodes examined and for the other 10 patients it is known that they did not undergo radical surgical resection.

Overall, the number of lymph nodes examined ranges from 0 to 135. More detail on the distribution of this QCI is shown in Table 57 (per size-grouped center) and Figure 54 (a box plot per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1.

As this upper boundary is very large and far away from what is supposed to be common practice, we have censored this QCI by setting all numbers examined larger than 25 lymph nodes equal to 25. Table 58 (per size-grouped center) and Figure 54 (a box plot per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1 show the distribution of the number of lymph nodes examined, per participating center, for the censored version of this QCI. From this we observe substantial differences between the centers concerning the number of lymph nodes examined.

2.8.5.3 Identification of relevant prognostic factors

We find significant univariate associations between this censored QCI and four prognostic factors, as shown in Table 126. The interpretation of the effects is as described in Table 81.

Table 126: Estimated coefficients [95% confidence interval] and corresponding p-value from the univariate linear regression models for QCI 1274 [#Nodes_Examined], considering all patients in the PROCARE database. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Coefficient [95% CI]	*p*-value	Joint *p*-vaue
Missing BMI [ref. = Not missing]	Missing	0.56 [0.03, 1.09]	0.04	
Tumor level [ref. = Missing]	Low	-0.39 [-1.80, 1.01]	< 0.0001	
	Mid	0.99 [-0.42, 2.40]		
	High	1.99 [0.52, 3.46]		
cStage [ref. = X/Missing]	I	-0.92 [-1.96, 1.94]	0.0002	
	II	-1.16 [-2.14, -0.19]		
	III	-0.54 [-1.38, 0.31]		
	IV	0.89 [-0.16, 1.94]		
Surgical technique [ref. = Missing]	TME	1.47 [-0.13, 3.08]	0.0006	
	PME	2.50 [0.82, 4.18]		

2.8.5.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 55 in Section 1). These center effects range between -7 and 7 'excess' mean number of lymph nodes examined. The P25 and P75 are located at -2 respectively 2 mean number of lymph nodes, hence the interquartile range on the mean excess number is 4 lymph nodes examined. In the caterpillar plot, we observe that four (merged) centers perform significantly above P75, i.e. the lower bound of their confidence interval is higher than P75, and three (merged) centers perform significantly below P25, i.e. the upper bound of their confidence interval is lower than P25.

2.8.6 Mesorectal (y)pCRM mentioned in the pathology report if radical surgical resection (QCI 1275, process)

2.8.6.1 Definition

N: Number of patients in the denominator for whom the mesorectal (y)pCRM was mentioned in the pathology report.

D: Number of patients treated with radical surgical resection and for whom a pathology report was completed.

Note that patients with (y)pStage 0 or (y)pStage X are excluded for analysis.

2.8.6.2 Description

There are 2615 (or 79%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 1932 (74%, or 71% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 59 (per size-grouped center) and Figure 56 (per participating center, after merging all centers with less than five

eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in one of the 67 (merged) centers to 100% in five (merged) centers. The funnel plot points to systematic variation between the centers.

2.8.6.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and nine prognostic factors, as shown in Table 127. The interpretation of the odds ratios is as described in Table 69.

Table 127: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1275 [pCRM_mm_Rep]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
BMI	(continuous)	0.99 [0.97, 1.01]	0.24	<0.0001
Missing BMI [ref. = Not missing]	Missing	0.45 [0.25, 0.81]	0.008	
Gender [ref. = Male]	Female	0.84 [0.70, 1.00]	0.05	
Tumor level [ref. = Low]	Mid	0.89 [0.72, 1.08]	<0.0001	
	High	0.57 [0.45, 0.73]		
	Missing	0.40 [0.25, 0.64]		
ASA score [ref. = I]	II	1.30 [1.04, 1.61]	<0.0001	
	III-V	1.33 [1.02, 1.74]		
	Missing	0.54 [0.40, 0.72]		
cStage [ref. = III]	I	0.59 [0.45, 0.77]	<0.0001	
	II	0.63 [0.49, 0.80]		
	IV	0.58 [0.44, 0.75]		
	Missing / X	0.44 [0.33, 0.58]		
Mode of surgery [ref. = Elective/Sch.]	Urgent / Emergency	0.58 [0.32, 1.04]	0.08	
	Missing	0.67 [0.39, 1.18]		
Ventral tumor [ref. = No]	Yes	1.04 [0.84, 1.28]	0.0001	
	Missing	0.62 [0.49, 0.78]		
cCRM positive [ref. = No]	Yes	2.00 [1.22, 3.28]	<0.0001	
	Missing	0.80 [0.53, 1.20]		
Surgical technique [ref. = PME]	TME	1.70 [1.38, 2.10]	<0.0001	
	Missing	0.64 [0.38, 1.07]		

2.8.6.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 56 in Section 1). These center effects range between -70% and 24% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -74% and 26% (since 74% of patients in the database achieved this QCI). The P25 and P75 are located at -11% resp. 12%, hence the interquartile range is 23%. In the caterpillar plot, we observe that four (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25. We also observe that one (merged) center performs significantly above P75, i.e. the lower bound of its confidence interval is higher than P75.

2.8.7 Tumor regression grade (Dworak) mentioned in the pathology report (after long course neoadjuvant treatment) (QCI 1276, process)

2.8.7.1 Definition

N: Number of patients in denominator having their tumor regression grade mentioned in the pathology report.

D: Number of patients treated with neoadjuvant long course radio(chemo)therapy and surgery (incl. any type of 'local excision').

2.8.7.2 Description

There are 1427 (or 43%) of the 3318 patients in the PROCARE database who meet the criteria in the denominator and are hence eligible for this QCI. Of the eligible patients, 1069 (75%, or 69% unweighted) achieved the QCI. The proportion of patients that achieved the QCI is shown in Table 60 (per size-grouped center) and Figure 57 (per participating center, after merging all centers with less than five eligible patients in one overlapping center) in Section 1. This proportion ranges from 0% in three of the 54 (merged) centers to 100% in four (merged) centers. The funnel plot points to systematic variation between the centers.

2.8.7.3 Univariate associations with prognostic factors

We find significant univariate associations between this QCI and five prognostic factors, as shown in Table 128. The interpretation of the odds ratios is as described in Table 69.

Table 128: Odds ratio estimate [95% Wald confidence interval] and corresponding p-value from the univariate logistic regression models for QCI 1276 [TRG_Rep]. For categorical variables, 'ref.' indicates the reference level.

Prognostic factor	Level	Odds ratio [95% CI]	*p*-value	Joint *p*-value
Age [ref. = < 70 years]	70+ years	1.31 [1.01, 1.69]	0.04	
BMI	(continuous)	0.96 [0.94, 0.99]	0.001	0.005
Missing BMI [ref. = Not missing]	Missing	0.29 [0.13, 0.62]	0.005	
cStage [ref. = III]	I	0.50 [0.26, 0.96]	<0.0001	
	II	0.91 [0.64, 1.30]		
	IV	0.55 [0.36, 0.83]		
	Missing / X	0.37 [0.23, 0.60]		
cCRM positive [ref. = No]	Yes	1.65 [0.92, 2.96]	0.0002	
	Missing	0.82 [0.49, 1.38]		
Surgical technique [ref. = PME]	TME	1.34 [0.92, 1.94]	0.06	
	Missing	0.71 [0.34, 1.47]		

2.8.7.4 Estimation of unadjusted center effects

Unadjusted center effects are shown in a caterpillar plot (Figure 57 in Section 1). These center effects range between -68% and 25% 'excess' probability. Note that the 'excess probabilities' are automatically constrained between -75% and 25% (since 75% of patients in the database achieved this QCI). The P25 and P75 are located at -23% resp. 17%, hence the interquartile range is 40%. In the caterpillar plot, we observe that six (merged) centers perform significantly below P25, i.e. the upper bounds of their confidence intervals are lower than P25.

APPENDIX 7: ACCURACY AND COMPLETENESS OF PROCARE DATABASE

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1 INTRODUCTION

Participation in PROCARE is on a voluntary basis. This means that the PROCARE database has no full coverage of rectal cancer patients in Belgium, because:

- Some centres do not participate
- Within participating centres, not every specialist, involved in the treatment of rectal cancer participates
- A participating specialist may not include certain cases in PROCARE

To get a better insight into the participation rate (completeness) and the degree of randomness in participation, the PROCARE database is linked with and compared to the BCR database.

The BCR database has full coverage of all new primary cancers in Belgium from 2004 onwards and in addition, this database provides information on topography, morphology, staging, and the centre that delivered the data. Therefore, the BCR database is the most suitable source to investigate the completeness of the PROCARE database.

The aim of this deliverable is to link and compare the PROCARE database with the BCR database in order to investigate the participation rate in general and per centre.

2 METHOD

2.1 PROCARE DATABASE

The rules for patients to be included in PROCARE are the following:

1. The lower limit of the tumour must be situated between 0 and 15 cm above the margo ani
2. Only adenocarcinoma are included
3. Only invasive tumours are included
4. Multiple synchrounous tumours are left out in PROCARE if it is indicated on the PROCARE data entry form. Note that before January 2010, this was not mentioned on the data entry form, therefore, this exclusion criterion will not be considered for the present study.
5. Patients for whom the INSS is not indicated cannot be included in the PROCARE database system. People not residing in Belgium are not included in the PROCARE database.

For the present analysis, only PROCARE patients with year of incidence between 2005 and 2008 were selected, because the BCR data after 2008 are not yet available.

2.2 BCR DATA SELECTION

Data were selected from the BCR database in order to link as many PROCARE patients as possible to this database. In this initial selection ICD-10 codes C18 (colon) and C19 (rectosigmoid) and all morphologies were included because:

- In PROCARE, all tumours more than 15 cm above the margo ani are regarded as (recto)sigmoid tumours, whereas in the BCR database, this limit is not so strictly interpreted in the coding practices and can be 17cm.
- The rectal tumour in PROCARE could be an extension from a tumour in the colon
- A tumour might be registered as colon, not otherwise specified in the BCR database when it is in fact a rectal tumour
- Some tumours with other morphologies than adenocarcinoma might have been included accidentally in PROCARE

2.3 LINKING AND FINAL SELECTION

The next step was to link the PROCARE database and the BCR selection and to select only those patients who fulfill the PROCARE criteria in the more strict sense. This was necessary to obtain a participation rate that is well interpretable. The full selection process is presented in figure 1.

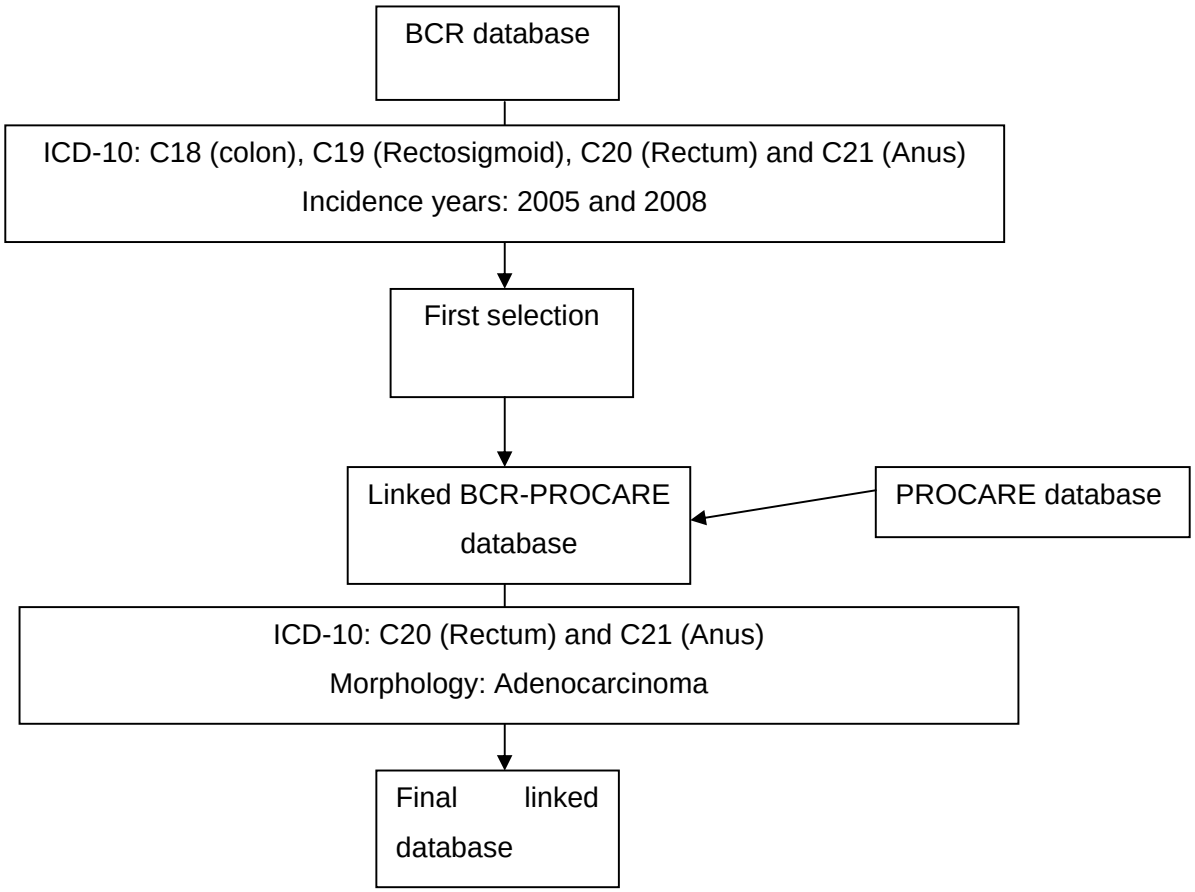


Figure 1. Process of selecting and linking databases

2.4 ANALYSIS PER CENTRE

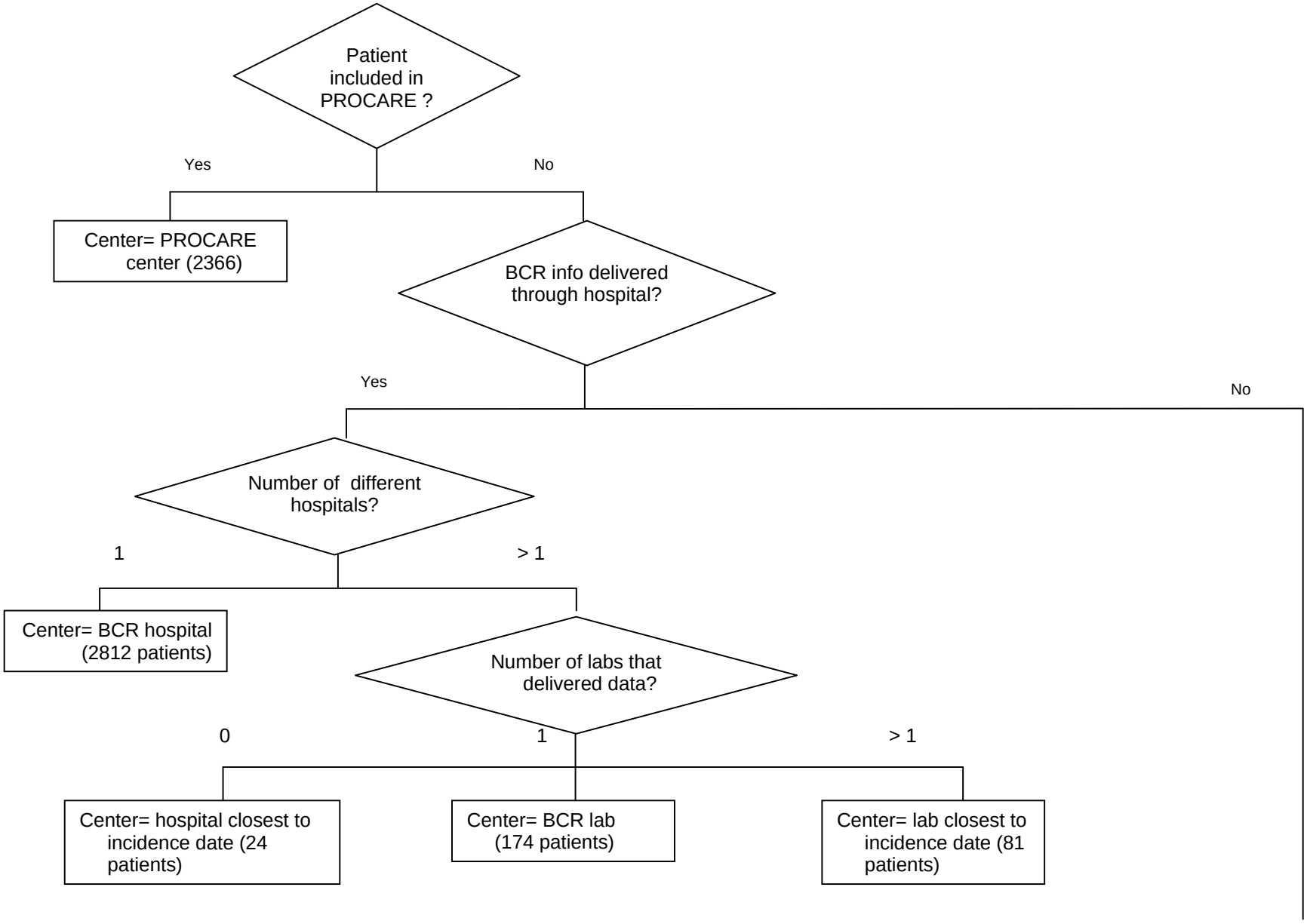
In PROCARE, the decision rule to assign a patient to a centre is based on the medical specialism that delivered the data. In case a patient has been operated, the centre of surgery is chosen, if this is missing, the centre in which the pathological examination is performed is chosen, and if this still yields no centre, the centre of chemotherapy is chosen. If no surgery is performed, then the centre of chemotherapy is chosen.

In the BCR database, it is less clear which speciality has delivered data. BCR data comes from multiple sources:

- in the clinical network, hospitals register all new cancer diagnosis and transfer them either directly to the Cancer Registry, either through the sickness funds and then to the Cancer Registry

- laboratories for pathological anatomy register every (pre-) malignant diagnosis and tranfser these data (electronically) to the Cancer Registry

This means that tumour data of the same patient can be delivered through multiple sources. Therefore we first defined an algorithm to assign a patient to a centre (figure 2).


Patient included in PROCARE ?
Yes
No
Center= PROCARE center (2366)
BCR info delivered through hospital?
Yes
No
Number of different hospitals?
1
> 1
Center= BCR hospital (2812 patients)
Number of labs that delivered data?
0
1
> 1
Center= hospital closest to incidence date (24 patients)
Center= BCR lab (174 patients)
Center= lab closest to incidence date (81 patients)

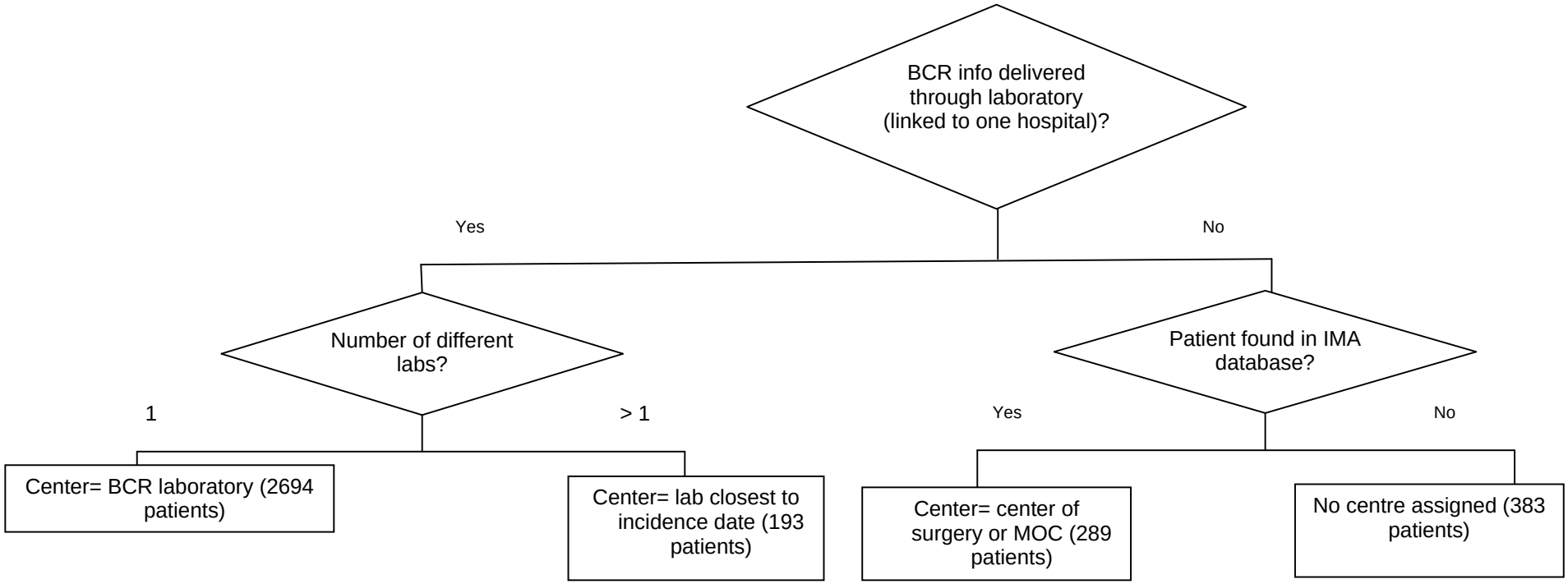


Figure 2. Algorithm to assign a patient to a centre.

The algorithm should be read as follows. When the patient is present in PROCARE, then the PROCARE centre is chosen. When the patient is not in PROCARE, one of the BCR sources is chosen in the following way:

- If there is a hospital source, this is preferred above the laboratory source.
    - If there is only one hospital, then this hospital is the final source
    - If there are multiple hospitals, then the laboratory is considered
    - If there are multiple hospitals and no laboratory, the hospital that delivered data closest to the incidence date is selected
- If there is no hospital source or multiple hospital sources, then the laboratory is considered
    - If there is only one laboratory involved, then this laboratory is the final source
    - If multiple laboratories are involved, the laboratory that delivered the data closest to the incidence date is chosen
- If data are only delivered through the sickness funds or through a laboratory that is not linked to a hospital then the IMA database was consulted. Note that at this moment, the IMA database, available to the BCR is limited to patients, diagnosed in 2005 and 2006. In the IMA database, the centre of surgery was considered first and if missing, the centre where the multidisciplinary oncological consultation (MOC) was performed was chosen.

3 RESULTS

3.1 DATABASE DESCRIPTION

3.1.1 PROCARE database

Incidence year	Frequency	Percent
2005	247	9.52
2006	889	34.26
2007	782	30.13
2008	677	26.09
TOTAL	2595	100

Table 1. Overview of number of patients in PROCARE database per incidence year

Table 1 gives an overview of the PROCARE database for the incidence years 2005-2008. For incidence year 2005, only a limited number of patients were registered in the PROCARE database, because the prospective registration started in 2006. The number of cases with incidence year 2008 might be underestimated, because patients, diagnosed in 2008 were still registered after closure of the database for the present project.

3.1.2 BCR database – first selection

Table 2 gives an overview of the BCR selected patients. In total, 31029 patients in Belgium were diagnosed with a colorectal tumour between 2005 and 2008.

Table 2. Overview of initial BCR selection, used to verify the PROCARE inclusion criteria.

ICD-10	Incindence year				Total
	2005	2006	2007	2008	
Anus (C21)	122	126	128	133	509
	1.62	1.63	1.66	1.65	1.64
Colon (C18)	4905	5028	5052	5288	20273
	65.27	64.99	65.35	65.72	65.34
Rectum (C20)	2113	2299	2309	2354	9075
	28.12	29.71	29.87	29.26	29.25
Recto-sigmoid (C19)	375	284	242	271	1172
	4.99	3.67	3.13	3.37	3.78
Total	7515	7737	7731	8046	31029

3.2 LINKING PROCARE AND BCR

In total, 40 patients from the PROCARE database (1.54%) could not be found in the BCR database selection. From this group, five were foreigners.

The remaining 35 patient were traced in the full BCR database (with all cancers until 2008). These patients were not in our BCR selection (table 2), because:

- The incidence date in the BCR database is before 01/01/2005 (n=17)
    - The incidence date in PROCARE might be the date of surgery whereas the BCR has an incidence date, based on a biopsy, done prior to the resection.
    - The PROCARE date is the date of a local reccurence, although the tumour is registered in PROCARE as a primary tumour.
- The rectal tumour is considered as a metastatic localization of another primary tumour (e.g. kidney, liver) (n=7)
- The tumour is not considered as invasive in the BCR database (n=6)

- The patients are not in the BCR database (n=5)

From the PROCARE patients who could be linked to the BCR database selection, the following ICD-10 codes (Table 3) occured:

Table 3. Overview of ICD-10 codes, present in PROCARE

ICD-10	Frequency	Percent
Colon (C18)	109	4.19
Rectosigmoïd (C19)	71	2.67
Rectum (C20)	2359	92.51
Anus (C21)	16	0.63

As expected, most patients had an ICD-10 code for rectum or anus (93%). Rectosigmoid accounted for 2.7% and colon for 4.2%. Due to different decision rules in PROCARE and the BCR database, it is difficult to decide whether these patients should be included in PROCARE or not.

Furthermore, 2546 patients (99.7%) had an adenocarcinoma, three patients had a neuro-endocrine tumour and six patients had a squamous cell carcinoma. These nine patients will be checked and possibly excluded from the PROCARE database in the future.

3.3 COMPLETENESS OF THE PROCARE DATABASE

To examine the completeness of the PROCARE database, a final selection was made of those patients with ICD code C20-C21 and an adenocarcinoma in the BCR database (PROCARE inclusion criteria).

The completeness of the PROCARE database per year of incidence is presented in table 4. When 2005 is ignored (the prospective registration has started in 2006, only few centres have retrospectively registered patients of 2005), the completeness of the PROCARE database is around 30%. Also note that up until now, cases of 2008 are still registered, so that the actual proportion of 2008 might be an underestimation.

Table 4. Proportion of PROCARE patients in BCR database.

Incidence year	N in PROCARE	N in BCR database	% coverage

2005	239	2091	11.4
2006	792	2287	34.6
2007	717	2298	31.2
2008	618	2340	26.4
Total	2366	9016	26.2

Next, it was investigated which stages, as registered in the BCR were best represented in the PROCARE database (Table 5-6). The cases from the incidence year 2005 as well as stage 0 cases were not included for the analyses per stage.

For cStage I and II the proportion present in PROCARE is little less than 40%, whereas for stage III, this increases to nearly 48%. From the stage IV patients, only 25% were present in the PROCARE database. This was expected given that PROCARE has a firm surgical background and many stage IV patients did not undergo surgery. Twenty percent of patients with an unknown cstage in the BCR database were registered in PROCARE.

For pStage, the picture is similar, although the distribution between stage I, II and III is more equal.[1]

Table 5. Proportion of PROCARE patients in BCR database – per cStage (2005 not included)

cStage	N in PROCARE	N in BCR database	% coverage
I	212	563	37.7
II	313	813	38.5
III	810	1690	47.9
IV	194	781	24.8
NA	8	54	14.8
X	588	3021	19.5
TOTAL	2125	6922	30.7

Table 6. Proportion of PROCARE patients in BCR database – per pStage (2005 not included)

pStage	N in PROCARE	N in BCR database	% coverage
I	501	1327	37.8
II	472	1322	35.8
III	576	1605	35.9
IV	97	388	25
NA	8	54	14.8
X	471	2226	21.2
TOTAL	2125	6922	30.7

[1] Patients who have ypstage 0 in the PROCARE database, are registered in the BCR database with pStage X (88.7%), pStage I (6.7%), pStage II (2.1%) and pStage III (2.6%) respectively.

Next, both databases were compared on age and sex. The mean age of the patients in the PROCARE database (67.0 years) was lower than the mean age of the patients who were only in the BCR database and not in the PROCARE database (69.9 years). This difference was significant $t(9013)=10.14$ ($p<.001$).

Furthermore, there were 61.9% male patients included in the PROCARE database. For the patients who were not included in this database, the percentage of men was 58.5%. This difference was also significant χ^2 (1) =8.74 ($p<.01$).

In conclusion, in the PROCARE database, the coverage of stage IV patients is lower, patients are on average younger, and the percentage of male patients is higher.

3.4 COMPLETENESS OF THE PROCARE DATABASE PER CENTRE

Table 7 gives an overview of the proportion of patients, present in PROCARE, per centre and per year of incidence. The total number of participating centres by the end of 2008 was 74. The number of centres, participating in PROCARE varies over time, with 56 in 2005, 66 in 2006, 61 in 2007 and 53 in 2008. The lower proportion of participating centres in 2008 can be explained by a number of centres who did not yet register their patients, diagnosed in 2008 by the time of closure of the database for the present project.

Table 7. Overview of proportion of patients included in PROCARE per centre

Year	2005			2006			2007			2008		
Centre	**Included**	**Total**	**%**	**Included**	**Total**	**%**	**Included**	**Total**	**%**	**Included**	**Total**	**%**
H001	1	8	12,5	7	12	58,3	2	4	50	8	14	57,1
H002	6	23	26,1	18	37	48,7	2	33	6,06	4	46	8,7
H003	0	14	0	4	7	57,1	5	19	26,3	0	11	0
H004	1	2	50	11	11	100	8	11	72,7	14	16	87,5
H005	0	18	0	21	26	80,8	23	28	82,1	19	25	76
H006	0	30	0	34	39	87,2	17	22	77,3	19	35	54,3
H007	0	20	0	1	20	5	16	28	57,1	12	25	48
H008	0	5	0	1	8	12,5	0	18	0	4	13	30,8
H009	4	29	13,8	14	31	45,2	8	27	29,6	18	31	58,1
H010	2	2	100	3	3	100				0	9	0
H011	7	23	30,4	15	21	71,4	6	18	33,3	1	26	3,85
H012	1	12	8,33	8	14	57,1	2	19	10,5	0	14	0
H013	4	16	25	8	10	80	7	12	58,3	14	22	63,6
H014	1	9	11,1	10	20	50	15	16	93,8	2	2	100
H015	6	34	17,7	9	29	31	11	28	39,3	17	38	44,7
H016	2	25	8	12	25	48	1	32	3,13	0	19	0
H017	7	63	11,1	13	45	28,9	20	66	30,3	11	75	14,7
H018	1	1	100	1	1	100						
H019	2	20	10	10	25	40	6	23	26,1	0	14	0
H020	5	50	10	21	38	55,3	23	34	67,7	5	43	11,6

H021	29	134	21,6	48	100	48	49	114	43	47	126	37,3
H022	2	4	50	9	11	81,8	3	11	27,3	4	10	40
H023	9	50	18	14	47	29,8	27	73	37	24	47	51,1
H024	2	20	10	10	31	32,3	11	33	33,3	10	31	32,3
H025	0	18	0	0	23	0	0	5	0	0	5	0
H026	7	33	21,2	15	42	35,7	7	19	36,8	8	17	47,1
H027	4	4	100	2	2	100				2	2	100
H028	6	51	11,8	2	40	5	0	46	0	0	40	0
H029	2	19	10,5	11	14	78,6	4	14	28,6	0	12	0
H030	2	10	20	4	8	50	0	3	0	0	2	0
H031	0	2	0	0	1	0	1	3	33,3	5	8	62,5
H032	4	16	25	6	13	46,2	7	7	100			
H033	5	13	38,5	19	37	51,4	19	29	65,5	22	31	71
H034	0	17	0	11	14	78,6	9	18	50	8	14	57,1
H035	14	49	28,6	29	66	43,9	25	50	50	28	39	71,8
H036	0	12	0	0	10	0	0	8	0	0	10	0
H037	7	39	18	48	58	82,8	51	57	89,5	33	49	67,4
H038	2	14	14,3	10	12	83,3	8	15	53,3	11	21	52,4
H039	2	15	13,3	11	14	78,6	9	12	75	3	6	50
H040	2	28	7,14	14	30	46,7	16	30	53,3	17	38	44,7
H041	4	10	40	5	11	45,5	1	4	25	0	9	0
H042	10	35	28,6	13	35	37,1	19	46	41,3	24	52	46,2
H043	0	10	0	2	15	13,3	0	8	0	0	12	0
H044	3	16	18,8	13	22	59,1	0	12	0	0	10	0
H045	0	13	0	5	16	31,3	3	12	25	6	17	35,3
H046	1	6	16,7	1	7	14,3	0	7	0	0	6	0
H047	17	59	28,8	37	73	50,7	29	44	65,9	23	41	56,1
H048	0	31	0	24	42	57,1	18	32	56,3	20	39	51,3
H049	0	3	0	0	3	0	1	22	4,55	0	7	0
H050	1	19	5,26	6	14	42,9	2	14	14,3	5	22	22,7
H051	0	49	0	2	42	4,76	28	52	53,9	7	35	20
H052	11	34	32,4	31	51	60,8	42	69	60,9	25	56	44,6
H053	0	9	0	0	3	0	0	2	0	4	9	44,4
H054	1	1	100	8	13	61,5	10	13	76,9	10	16	62,5
H055	0	10	0	0	12	0	0	20	0	1	13	7,69
H056	0	22	0	1	24	4,17	5	18	27,8	4	17	23,5
H057	3	15	20	7	9	77,8	8	14	57,1	12	20	60
H058	4	36	11,1	21	39	53,9	8	19	42,1	11	21	52,4
H059	0	8	0	0	16	0	1	17	5,88	4	10	40
H060	0	10	0	0	10	0	0	17	0	0	12	0
H061	2	39	5,13	25	44	56,8	26	56	46,4	15	51	29,4
H062	4	10	40	0	6	0						
H063	1	6	16,7	2	3	66,7	1	2	50			
H064	5	17	29,4	10	16	62,5	7	12	58,3	5	22	22,7
H065	2	3	66,7									
H066	3	22	13,6	11	27	40,7	14	19	73,7	13	27	48,2
H067	5	46	10,9	20	58	34,5	16	46	34,8	6	57	10,5
H068	1	21	4,76	6	22	27,3	10	22	45,5	22	31	71
H069	0	6	0	6	12	50	7	20	35	7	17	41,2
H070	1	7	14,3	5	15	33,3	3	13	23,1	4	17	23,5
H071	3	13	23,1	11	21	52,4	8	29	27,6	7	18	38,9
H072	1	19	5,26	5	53	9,43	1	49	2,04	0	45	0
H073	3	16	18,8	13	18	72,2	5	15	33,3	0	23	0
H074	1	13	7,69	1	12	8,33	4	9	44,4	3	16	18,8
H075	1	15	6,67	7	12	58,3	13	21	61,9	7	13	53,9
H076	3	10	30	12	16	75	7	17	41,2	0	12	0

H077	0	1	0	0	4	0	0	10	0	0	9	0
H078							0	1	0	0	2	0
H079	0	19	0	0	17	0	0	24	0	0	26	0
H084	0	4	0	0	8	0	0	1	0	0	15	0
H085	0	16	0	0	18	0	0	19	0	0	1	0
H088	0	4	0	0	5	0	0	6	0	0	5	0
H089	0	59	0	0	69	0	0	55	0	0	48	0
H090	0	9	0	0	10	0	0	7	0	0	25	0
H091	0	15	0	0	21	0	0	23	0	0	22	0
H092	0	31	0	0	49	0	0	43	0	0	41	0
H093							0	5	0	0	10	0
H095	0	21	0	0	12	0				0	1	0
H096	0	9	0	0	5	0						
H097	0	5	0	0	7	0						
H098	0	12	0	0	5	0	2	2	100	3	5	60
H099	0	16	0	0	14	0	0	17	0	0	12	0
H100	0	5	0	0	13	0	0	4	0	0	8	0
H101	0	52	0	0	44	0	0	44	0	0	42	0
H102	0	59	0	0	70	0	0	66	0	0	73	0
H103	0	1	0									
H104	0	6	0									
H106	0	12	0	0	20	0	0	16	0	0	10	0
H107										0	3	0
H108	0	2	0	0	2	0	0	2	0	0	2	0
H109	0	2	0							0	6	0
H110	0	12	0	0	25	0	0	21	0	0	24	0
H111	0	15	0	0	12	0	0	13	0	0	10	0
H112	0	17	0	0	8	0	0	13	0	0	16	0
H113	0	130	0	0	11	0	0	26	0	0	19	0
Total	239	2028	11.8	792	2236	35,5	717	2175	32.9	618	2194	28,1

4 CONCLUDING REMARKS

Using the BCR database, we were able to examine the completeness of the PROCARE database. However, the interpretation of the results has to be performed with great caution due to the following reasons:

- When tumours are situated between 15 and 17cm above the margo ani, they are considered as rectal tumours in the BCR database, but they are excluded in PROCARE.
- Patients who are not treated are not included in PROCARE. Furthermore, a number of centres only register surgically treated patients, meaning that patients who did not have surgery are not registered.
- There is no deadline in PROCARE to register patients. A number of patients with incidence year 2008 were added to the database after closure for the present project.
- Assigning a patient to a centre is done differently in the BCR database, compared to the PROCARE database. This might cause problems, especially when a patient is treated in multiple centres.

In the future, administrative databases, such as the IMA database may help to overcome some of these problems.

Appendix 8: Further detail on the construction of adjusted excess probabilities for aggregated quality indexes

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1 ADJUSTMENT OF EXCESS PROBABILITIES

1.1 PROTOCOL HIERARCHICAL STEPWISE FORWARD SELECTION PROCEDURE

A model building procedure –i.c. a logistic regression model with Firth's bias correction - is performed to predict an aggregated all-or-none quality score from the center and patient-level characteristics.

1.2 SUMMARY MODEL BUILDING PROCEDURE:

We will adjust all-or-none scores for baseline patient characteristics as was done for outcome QCI's. Specifically, we conduct a Stepwise procedure as follows:

1) Adjustment for main effects of age (continuous, with breakpoint after 70 years) and gender enter the model first

2) We build a main effects model, allowing the following variables to enter: BMI with an indicator of its missingness, and the 9 categorical variables including a category for missingness: cSTAGE, ASA co-morbidity score, level of the tumor, mode of surgery, ventral tumor, cCRM, cT4, pre-operative incontinence, surgical technique.

Table 1: Summary: levels of prognostic factors

Effect	Levels
BMI (continuous)-	
BMI missing [ref. = Not missing]	Missing
Cstage [ref=I]	II, III, IV, missing
ASA score [ref. = I]	II, III-V, missing
Tumor level [ref. = Low]	Mid, High, Missing
Mode of surgery [ref. = Elective/Scheduled]	Urgent / Emergency, missing
Ventral tumor [ref. = No]	Yes, missing
cCRM positive [ref. = No]	Yes, missing
cT4 [ref. = No]	Yes, missing
Preoper. incontinence [ref. = No]	Yes, missing
Surgical technique [ref. = PME]	TME, missing

After adding significant main effects in a stepwise forward manner (with significance level 0.05 for entering the model and 0.1 for leaving the model), significant interactions from among the main effects are added, again in a stepwise forward manner (with significance level 0.05 for entering the model and 0.1 for leaving the model).

Note: Missingness has been observed mainly for the factors cCRM positive, BMI, ventral tumor, and -ASA-score (more than 20% missingness, see Table 1).

Table 2: Number of patients with missing values in the adjustment factors

Effect	N Patients missing	%
cCRM positive	2706	82%
BMI	1241	37%
Ventral tumor	832	25%
ASA score	689	21%
Cstage (XM)	495	15%
Mode of surgery	455	14%
Surgical technique	455	14%
cT4	421	13%
Preoper. incontinence	333	10%
Tumor level	319	10%

2 DOMAIN 1 'GENERAL QUALITY INDICATORS'

2.1 CALCULATING SCORES BASED ON A BINARY QI FOR QCI1111

All-or-none scores for this domain are based on overall survival (QCI 1111) in general and on the probability to survive 3 years or longer in particular. When QCI1111 is the sole contributor to the aggregated domain, the (3 year) survival probability is derived directly from the Cox-model fit. When (3 year) survival is combined with binary quality indicators in a binary all-or-none score, we impute a binary outcome for 3 year survival in the set of 1279 patients who was not observed to die and followed for less than 3 years. For the current exercise, the imputation model starts form the conditional probability of surviving 3 years, given baseline covariates and how long one was observed to survive so far. In general it may be advantageous to allow for time-varying covariates to influence the imputation model. We impute 10-fold here from the Cox proportional hazards model, built in a forward stepwise manner with the same factors considered for the all-or-none score models. For illustration purposes, and in the interest of time, the model was built separately on the first 3 imputed datasets before deciding on a common model fit to all imputed datasets leading to averaged estimates of the excess center-specific probabilities.

2.2 COX MODEL FOR IMPUTATION OF (3 YEAR) SURVIVAL (QCI 1111)

The most significant factor in a proportional hazards model corrected for confounding by age and gender is asa score. ($p<.0001$). Next, the factors "Mode of surgery" ($p<.0001$) and "cT4" ($p=.0029$) enter the model. No other factors have added further 'significant' value to this model (smallest p-value is .095).

2.3 MAIN EFFECTS MODELS

The following exercise on the analysis of 3 year survival with imputed outcomes, is for illustrative and comparative purposes since we do not need the imputations for a single score. Also, it should be emphasized that as the dataset matures, fewer and fewer imputations should be necessary so that their impact is reduced.
In view of an aggregated all-or-none score we start by estimating adjusted center effects based on each of the first three datasets with imputed 3-year survival probabilities.

2.3.1 Main effects based on ”imputed” score 1

The most significant factor in a model corrected for confounding by age and gender is c-stage. (p<.0001). Next, the factors “asa score” (p<.0001), “Mode of Surgery” (p<.0001), “cT4” (p=.0013), “Ventral Tumor” (p=.0016), “preop. Incont.” (p=0.040) enter the model. No other factors enter the model (smallest p-value is 0.063).

2.3.2 Main effects based on ”imputed” SCORE 2

The most significant factor in a model corrected for confounding by age and gender is c-stage. (p<.0001). Next, the factors “asa score” (p<.0001), “Mode of Surgery” (p<.0001), “cT4” (p=.0020), “Ventral Tumor” (p=.0054), “preop. Incont.” (p=0.024) enter the model. No other factors enter the model (smallest p-value is 0.090).

2.3.3 Main effects based on ”imputed” SCORE 3

The most significant factor in a model corrected for confounding by age and gender is c-stage. (p<.0001). Next, the factors “asa score” (p<.0001), “Mode of Surgery” (p<.0001), “cT4” (p=.0039), “preop. Incont.” (p=0.024) and “Ventral Tumor” (p=.022), enter the model. No other factors enter the model (smallest p-value is 0.36).
The final adjustment models for score 1-3 are identical; the only exception is that factors “ventral tumor” and “preop incont” enter the model in reverse order in score 2 vs. score 3 models. In the interest of time. one decides to test for significant interactions between main effects based on the significant main effects in the dataset 1.

2.4 INTERACTIONS BETWEEN MAIN EFFECTS (IMPUTED DATASET 1)

Subsequently, interactions are added to the model with main effects for age (with a different slope before and after the breakpoint of 70 years), gender, c-Stage, ASA-score, Mode of Surgery, cT4, ventral tumor and preoperative incontinence.

Table 3: Interactions Domain 1

age [cont] - ASA score [ref=I]
age [cont] -cStage [ref=1]
age [cont] -cT4 [ref = No]
age [cont] - gender [ref. = Male]
age[cont] - ModeOfSurgery[ref.=Elect./Sched.]
age[cont] - vent.Tumor[ref=No]
ASAscore[ref=I] - cStage[ref=1]
ASAscore[ref=I] - cT4[ref=No]
ASAscore[ref=I] - gender[ref.=Male]
ASAscore[ref=I] - ModeOfSurgery[ref.=Elect./Sched.] - ModeOfSurgery[ref.=Elect./Sched.]
ASAscore[ref=I] - vent.Tumor[ref=No]
cStage[ref=1] - cT4[ref=No]
cStage[ref=1] - gender[ref.=Male]
cStage[ref=1] - ModeOfSurgery[ref.=Elect./Sched.]
cStage[ref=1] - vent.Tumor[ref=No]
cT4[ref=No] - gender[ref.=Male]
cT4[ref=No] - ModeOfSurgery[ref.=Elect./Sched.]
cT4[ref=No] - vent.Tumor[ref=No]
gender[ref.=Male] - ModeOfSurgery[ref.=Elect./Sched.]
gender[ref.=Male] - vent.Tumor[ref=No]
ModeOfSurgery [ref. = Elect./Sched.] - vent.Tumor [ref = No]

Convergence was not attained for interactions with the missing level of factor “preop. Incont.” And for interactions between cT4 and cStage (cstageII by cT4_missing, cstage_missing(XM) by cT4_”yes”, cstage_missing(XM) by cT4_missing). In a model with the most significant interaction “asa-cT4”, the factor preop_incont is no longer significant (p=0.24) and leaves the model. Next “ASA-gender” enters the model (p=0.040) and no other factors can be added (smallest p-value is 0.16).

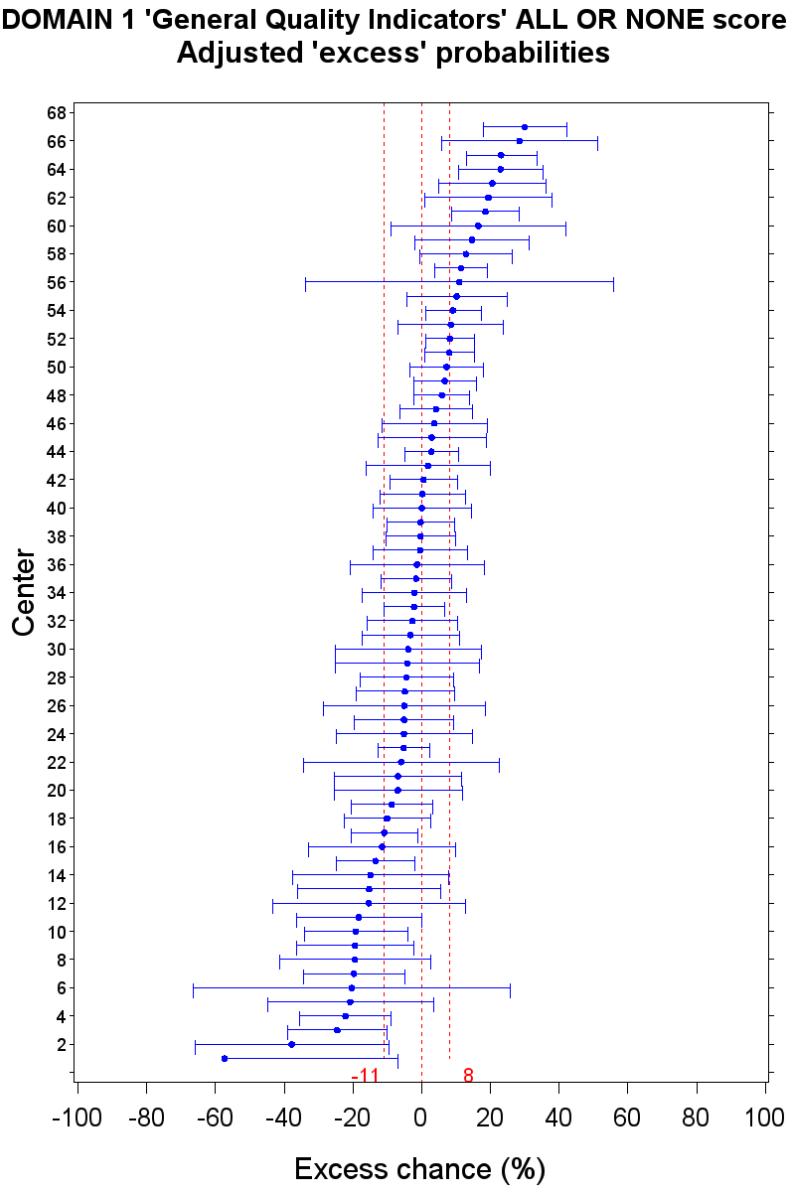
Hence, our final model adjusts for age (with a different slope before and after the breakpoint of 70 years), gender, ASA, mode of surgery, cT4 and ventral tumor with the 2 interaction effects “ASA score by cT4” and “ASA-score by Gender”.

We finally apply this common model to calculate the adjusted centre-specific excess probabilities based on an average of 10 “imputed” score models.

2.5 ALL-OR-NONE SCORE DOMAIN 1

A first assessment of the discriminating ability between centers of this adjusted “all-or-none” score is made by examining the caterpillar plot of excess probability in Figure 2. In this caterpillar plot we find no centers performing ‘significantly’ below P25 (11%) and 4 centers above P75 (8%).

Figure 1: Caterpillar plot of the adjusted center-specific 'excess' probability for the "all-or-none" domain 1 score



3 DOMAIN 2 'DIAGNOSIS AND STAGING' AGGREGATION

3.1 MAIN EFFECTS

The most significant factor in a model corrected for age and gender is Tumour Level. (p<.0001). Next, the factor "Mode of surgery" enters the model (p<.0001) and in order: cT4 (p=0.0016) and cStage (p=0.018). No other factors have added further 'significant' value to this model.

3.2 INTERACTIONS BETWEEN MAIN EFFECTS

Next, interactions are added to the model with main effects for age (with a different slope before and after the breakpoint of 70 years), gender, tumour level, mode of surgery, cT4 and cStage.

Table 4: Interactions examined for Domain 2

age[cont.] - cStage[ref=I]
age[cont.] - cT4[ref=No]
age[cont.] - gender[ref=male]
age[cont.] - modeofsurgery[ref=Sched.]
age[cont.] - tumorlevel[ref=Low]
cStage[ref=I] - cT4[ref=No]
cStage[ref=I] - gender[ref=male]
cStage[ref=I] - modeofsurgery[ref=Sched.]
cStage[ref=I] - tumorlevel[ref=Low]
cT4[ref=No] - gender[ref=male]
cT4[ref=No] - modeofsurgery[ref=Sched.]
cT4[ref=No] - tumorlevel[ref=Low]
gender[ref=male] - modeofsurgery[ref=Sched.]
gender[ref=male] - tumorlevel[ref=Low]
modeofsurgery[ref=Sched.] - tumorlevel[ref=Low]

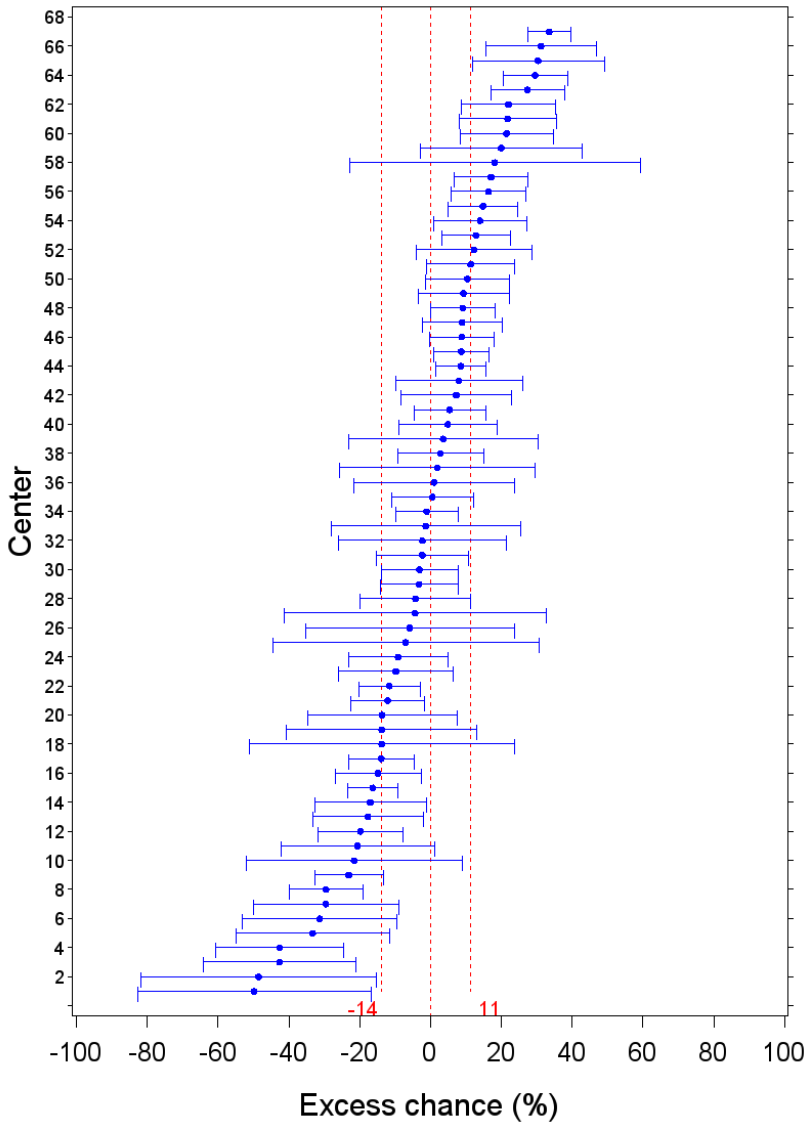
The most significant interaction was “Age-gender” (p=0.033) followed by “gender by cStage” (p-value: 0.023). No further interactions contributed significantly (smallest p-value is 0.12)

Hence, our final model adjusts for age (with a different slope before and after the breakpoint of 70 years), gender, Tumor Level, cT4 and cStage with the 2 interaction effects “Age by Gender” and “Gender by cStage”.

3.3 ALL-OR-NONE SCORE DOMAIN 2

A caterpillar plot of adjusted excess probabilities for the all-or-none score for “diagnosis and staging” is shown in Figure 2. We find 5 centers performing ‘significantly’ below P25 (-14%) and 5 above P75 (+11%).

Figure 2: Caterpillar plot of the adjusted center-specific 'excess' probability for the "all-or-none" domain 2 score



4 DOMAIN 3 'NEOADJUVANT TREATMENT' AGGREGATION

Since this domain is represented by a single QCI 1221, one refers to the unadjusted center effects that have been treated in Deliverable 6.

5 DOMAIN 4 'SURGERY' AGGREGATION

5.1 MAIN EFFECTS

The most significant factor entering a model corrected for main effects of age and gender is Tumour level ($p<0.0001$) The factor "surgery" enters next ($p<0.0001$) and then in order "mode of surgery" ($p<0.0001$), "cT4" ($p<0.0001$) , mode of surgery

(p<0.0001), cCRM (p=0.0009), cStage (p=0.0051), Ventral Tumor (p=0.0088) and ASA score (p=0.017). No other factors are significant at the .05 level (smallest p-value is 0.078). Our final model is left with 10 main effects (Age, gender, Tumour level, surgery, mode of surgery, cT4, cCRM, cStage, Ventral Tumor, ASA score).

5.2 INTERACTIONS BETWEEN MAIN EFFECTS

Subsequently, interactions between the main effects are added to the model:

Table 5: Interactions examined for Domain 4

age[cont.] - ASA[ref=I]
age[cont.] - cCRM[ref=No]
age[cont.] - cStage[ref=I]
age[cont.] - cT4[ref=No]
age[cont.] - gender[ref=male]
age[cont.] – mode of surgery[ref=Sched.]
age[cont.] - surgery[ref=PME]
age[cont.] – tumor level[ref=Low]
age[cont.] – ventral Tumor[ref=No]
ASA[ref=I] - cCRM[ref=No]
ASA[ref=I] - cStage[ref=I]
ASA[ref=I] - cT4[ref=No]
ASA[ref=I] - gender[ref=male]
ASA[ref=I] – mode of surgery[ref=Sched.]
ASA[ref=I] - surgery[ref=PME]
ASA[ref=I] – tumor level[ref=Low]
ASA[ref=I] – ventral Tumor[ref=No]
cCRM[ref=No] - cStage[ref=I]
cCRM[ref=No] - cT4[ref=No]
cCRM[ref=No] - gender[ref=male]
cCRM[ref=No] – mode of surgery[ref=Sched.]
cCRM[ref=No] - surgery[ref=PME]
cCRM[ref=No] – tumor level[ref=Low]
cCRM[ref=No] – ventral Tumor[ref=No]
cStage[ref=I] - cT4[ref=No]
cStage[ref=I] - gender[ref=male]
cStage[ref=I] – mode of surgery[ref=Sched.]
cStage[ref=I] - surgery[ref=PME]
cStage[ref=I] – tumor level[ref=Low]
cStage[ref=I] – ventral Tumor[ref=No]
cT4[ref=No] - gender[ref=male]
cT4[ref=No] – mode of surgery[ref=Sched.]
cT4[ref=No] - surgery[ref=PME]
cT4[ref=No] – tumor level[ref=Low]
cT4[ref=No] – ventral Tumor[ref=No]
gender[ref=male] – mode of surgery[ref=Sched.]
gender[ref=male] - surgery[ref=PME]
gender[ref=male] – tumor level[ref=Low]
gender[ref=male] - ventralTumor[ref=No]
modeofsurgery[ref=Sched.] - surgery[ref=PME]
modeofsurgery[ref=Sched.] – tumor level[ref=Low]
modeofsurgery[ref=Sched.] – ventral Tumor[ref=No]
surgery[ref=PME] – tumor level[ref=Low]
surgery[ref=PME] – ventral Tumor[ref=No]
Tumor level[ref=Low] – ventral Tumor[ref=No]

We add interaction terms starting from the model with the interaction “ASA score by Mode of surgery” (which is most significant among the 45 interactions, p<0.0001), “cStage by ventralTumour” (p=0.023). Adding other interactions does not improve the model (smallest p-value is 0.0504).

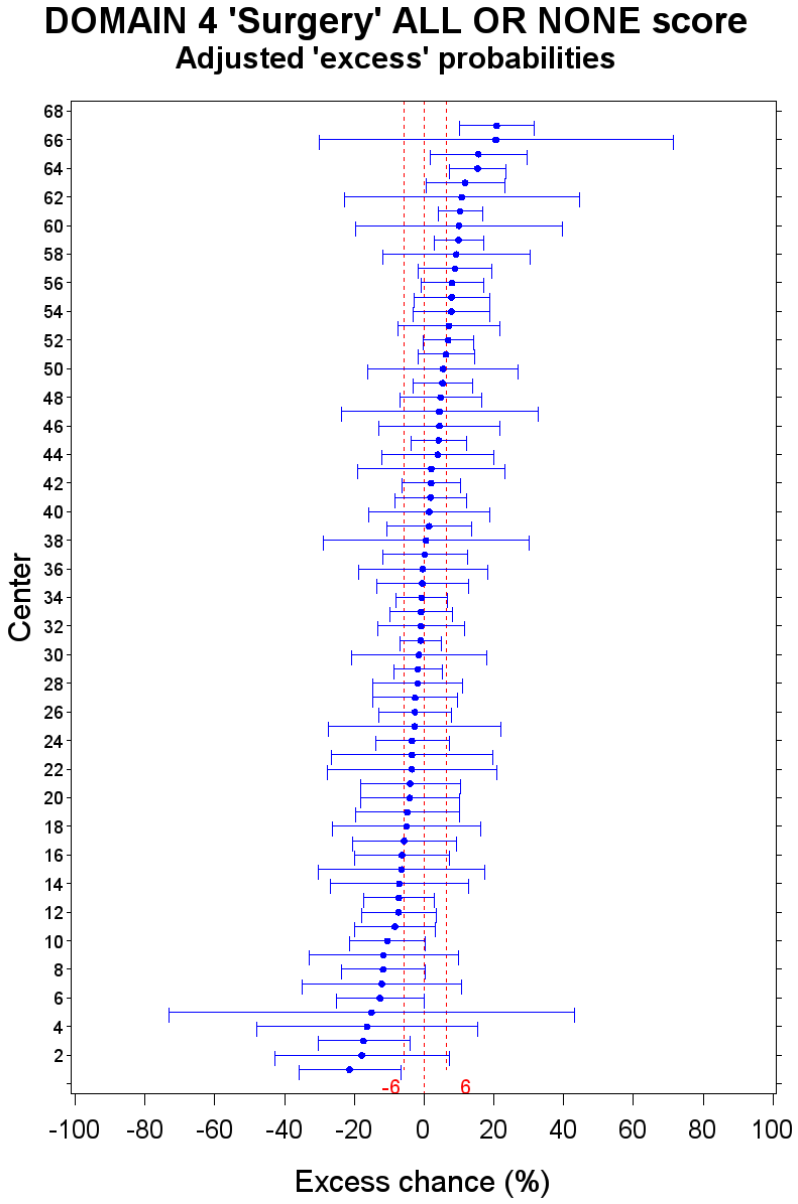
It was not possible to assess significance of interaction effects for all combination of levels, i.c. one lacks sufficient data to assess the interaction of ASA score level Missing by all cStage levels and surgery technique Missing, cT4 Missing by cCRM “Missing” and cstage Missing by all levels of cT4, ASA score III by Surgery technique Missing, cStage II by Surgery Technique Missin, asaIII by surgery Missing, cStageII by cT4 Missing and Mode of surgeryEM by ventralTumor “Yes”.

Hence, our final model will adjust for age (with a different slope before and after the breakpoint of 70 years), gender, Tumour level, surgery, mode of surgery, cT4, cCRM, cStage, Ventral Tumor, ASA score and 2 interactions 1) “ASA score by Mode of surgery” and 2) ”cStage by ventralTumour”.

5.3 ALL-OR-NONE SCORE DOMAIN 4

Adjusted center effects are shown in the caterpillar plot (see Figure 4**Error! Reference source not found.**)where we find one center performing ‘significantly’ below P25 (-6%) and two centers significantly above P75 (6%), where we find one center performing ‘significantly’ below P25 and 2 above P75.

Figure 3: Caterpillar plot of the adjusted center-specific 'excess' probability for the "all-or-none" domain 4 score.



6 DOMAIN 8 'HISTOPATHOLOGIC EXAMINATION' AGGREGATION

6.1 MAIN EFFECTS

The most significant factor in a model corrected for confounding by age and gender is "mode of surgery". (p<0001) The factor "cStage" is the best factor in a model with gender, age and mode of surgery (p<0001). Addition of factor "surgery" (p=0.04322) yields a model with 3 additional effects to adjust for (no factors leave the model). Adding other factors does not add further 'significant' value to the model (all p ≥ .07).

6.2 INTERACTIONS BETWEEN MAIN EFFECTS

Subsequently, interactions are added to the main effects:

Table 6: Interactions Domain 8

age [cont]- cstage [ref=I]
age [cont] - gender [ref. = Male]
age [cont] - mode_of_surgery [ref. = Elective/Sch.]
age [cont] - surgical technique [ref. = PME]
cstage [ref=I] -gender [ref. = Male]
cstage [ref=I] - mode_of_surgery [ref. = Elective/Sch.]
cstage [ref=I] -surgical technique [ref. = PME]
gender [ref. = Male] - mode_of_surgery [ref. = Elective/Sch.]
gender [ref. = Male] - surgical technique [ref. = PME]
mode_of_surgery [ref. = Elective/Sch.] - surgical technique [ref. = PME]

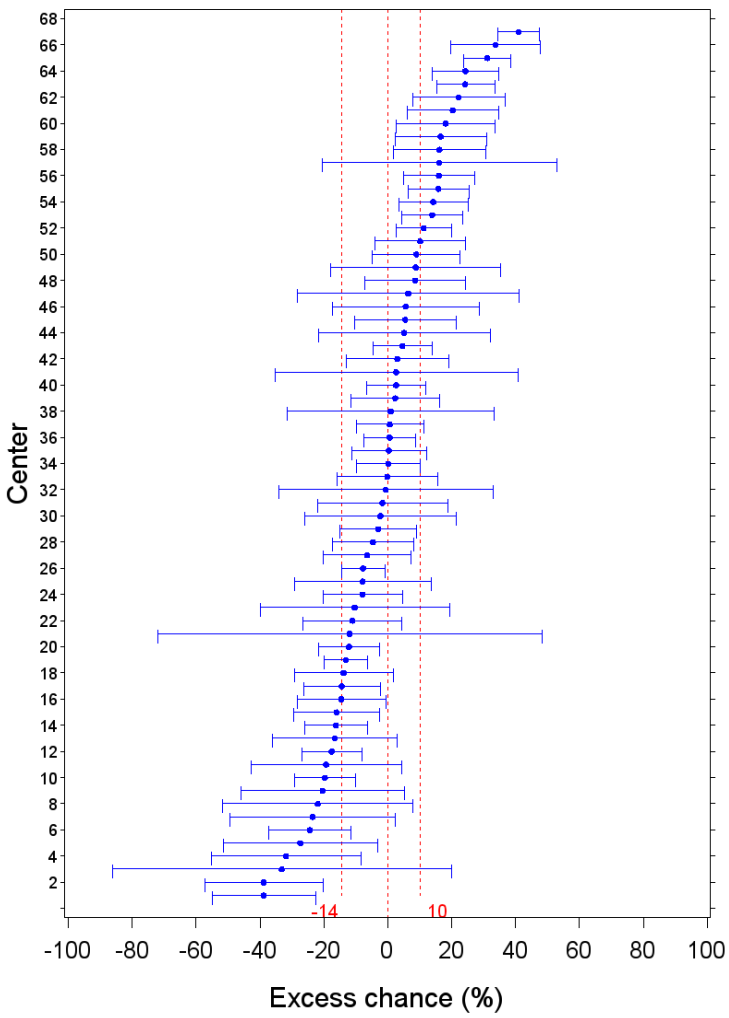
Now we add interaction terms starting from the model with the interaction "mode of surgery-surgery" (which is most significant among the 10 interactions, p<.0001), then enters "cStage by gender" (p=.044) among 9 remaining interactions. Other interactions do not enter the model (smallest p-value is 0.50).

Hence our final model contains main effects age, gender, "mode-of-surgery", "c-Stage", "surgery technique" together with 2 interaction effects, i.e.
"mode of surgery by surgery technique" and "cStage by gender".

6.3 ALL-OR-NONE SCORE DOMAIN 8

A first assessment of the discriminating ability between centers of this "all-or-none" score is made by examining the caterpillar plot of the excess probability in Figure 4. In this caterpillar plot we find 2 centers performing 'significantly' below P25 and 5 above P75.

Figure 4: Caterpillar plot of the adjusted center-specific 'excess' probability for the "all-or-none" domain 8 score



7 COMPOSITE SCORE AGGREGATION

We constructed a **composite** index for outcome and process QCIs combined. We appreciated this is a complex measure to interpret and produced it in response to the request to arrive at a single global quality index. The relative weight of outcome and process QCIs in this construction is to some degree a matter of choice. In an attempt to give similar chances to outcome and process QCIs to enter, the first approach starts from the previously selected QCIs for respectively outcome and process aggregated scores. The second approach starts instead from all available QCIs with sufficient data quality. The second approach was developed in the main report and kept as the approach of choice. The first one is detailed below.

7.1 COMPOSITE ALL-OR-NONE SCORE BASED ON THE 4 PROCESS AND 3 OUTCOME QCIS

7.1.1 List of candidate QCIs

Previously the combined **outcome** QI was constructed using an all-or-none score involving the following QCIs:

- QCI 1111: Overall survival [cut-off at 3 years]
- QCI 1231: Proportion of R0 resections
- QCI 1234b: Postoperative major surgical morbidity with reintervention under narcosis after radical surgical resection.

The combined **process** QI was constructed using the all-or-none score involving the following QCIs:

- QCI 1217: Time between first histopathological diagnosis and first treatment [cut-off at 30 days].
- QCI 1232a: Proportion of APR- Hartmann's procedure or total excision of colon and rectum with definitive ileostomy. [Negative QCI]
- QCI 1273: Distal tumour-free margin mentioned in the pathology report.
- QCI 1274: Number of lymph nodes examined [cut-off at 10].

7.1.2 Concurrent validity of selected QCIs

To examine the concurrent validity we performed a principal component analysis on the 'excess' probabilities for QCIs 1111, 1231, 1234b, 1217, 1232a, 1273 and 1274.

The eigenvalues of the correlation matrix and the proportion of the total variation in the data that could be explained by each factor are presented in Table 7.

Table 7: Eigenvalues and (cumulative) percentage of variance explained by principal components of the center-specific 'excess' probabilities of the seven selected outcome and process QCIs (on n =60 centers for which there were at least 5 eligible patients for all these QCIs).

Dimension	Eigenvalue	Proportion	Cumulative
1	1.62	0.23	0.23
2	1.27	0.18	0.41
3	1.03	0.15	0.56
4	0.95	0.14	0.70
5	0.88	0.13	0.82
6	0.69	0.10	0.92
7	0.56	0.08	1.00

The PCA confirms that there is not one single dimension underlying the seven indicators. The main dimension (factor 1) accounts for 23% of the overall variance for the seven indicators. The second factor accounts for an additional 18%. Based on the default statistical selection criterion of eigenvalues greater than 1, 3 dimensions are retained. Note that the proportions in the third column of Table 7 indicate that three factors account for only 56% of the information available among these QCIs. Therefore we decided to take 4 dimensions into account with a total explained variance of 70%. The (quartimax rotated) loadings of the QCIs on these dimensions are presented in Table 8.

Table 8: Quartimax rotated factor loadings of the QCIs on the four first dimensions in the PCA for the center-specific excess probabilities of the seven selected QCIs (on n = 60 centers for which there were at least 5 eligible patients for all these QCIs).

	Factor1	Factor2	Factor3	Factor 4
e1111 [OS]	0.80	0.14	0.09	0.04
e1231 [%R0res]	0.86	-0.08	-0.02	-0.01
e1234b [%Major_morb]	0.00	-0.22	0.83	-0.19
e1217 [Time_histo_1ther]	0.19	-0.18	0.09	0.76
e1232a [%Defin_ostomy]	-0.15	0.19	-0.19	0.67
e1273 [%Dist_Margin_Rep]	-0.20	-0.51	-0.61	-0.24
e1274 [#Nodes_Examined]	0.02	0.87	-0.12	-0.04

From Table 8 we derive that the first dimension is mainly related to QCIs 1111 and 1231; dimension 2 consists mainly of QCI 1274. Factor 3 is mainly related to QCIs 1273 and 1234b. Dimension 4 is mainly related to QCIs 1217 and 1232a.

Now we further select based on clinical criteria and discriminating ability.

QCI1231 and QCI 1111 have comparable and very good data quality scores: QCI 1231 has a lower IQR than QCI 1111 (11% vs 14%) but has loadings on the first dimension that are slightly higher than QCI 1111 (0.86 vs 0.8). We choose QCI1111

as the clinically most relevant candidate to represent the first dimension. QCI 1274 is the only retained candidate for the second dimension. For the third dimension QCI 1234b has a lower PROCARE survey score of 2 on clinical importance, therefore QCI 1273 is chosen, although data availability is inferior to 1234b (72% vs 90% for QCI 1234b). QCI 1217 has poor data quality parameters and therefore 1232a is chosen as the representative for the fourth dimension.

7.1.3 Construction of the quality index (QI)

In summary, the composite QI will be constructed using the following QCIs:

- QCI 1111: Overall survival
- QCI 1232a: Proportion of APR- Hartmann's procedure or total excision of colon and rectum with definitive ileostomy.
- QCI 1273: Distal tumour-free margin mentioned in the pathology report.
- QCI 1274: Number of lymph nodes examined.

7.1.3.1 All-or-none score

The "all-or-none" score for the composite index indicates whether a patient reaches patient-level benchmarks, in this case:

- whether he/she survived 3-years since incidence of rectal cancer,

  For patients with a follow-up of less than 3 years, a model based multiple imputation technique is used to construct the all-or-none score and corresponding confidence limits. More details on multiple imputation are provided in Appendix 2.

- whether he/she did avoid the APR- Hartmann's procedure or total excision of colon and rectum with definitive ileostomy,
- whether he/she had a tumour-free margin mentioned in the pathology report, and
- whether there were at least 10 lymph nodes examined

Of the 3318 patients in the database, 3136 (94.5%) patients are eligible for at least one QCI in the QI, while 1881 (56.7%) are eligible for all (four) contributing QCIs.

Of the 3318 patients, 1270 (38.3%) patients achieved the all-or-none score or 44.5% (weighted), or 39.1% (unweighted) on average per center.

Unadjusted center effects are shown in the caterpillar plot (see Figure 5), where we find 4 centers performing 'significantly' below P25 (-9%) and 6 above P75 (+14%).

We ultimately opted for the other score because it had greater discriminating ability and because of the problems of interpretation associated with QCI1232a as explained below Table 35 in the main report.

Figure 5: Excess probabilities for the All-or-none score based on the 4 (out of 7) selected QCIs (with multiple imputation for QCI1111)

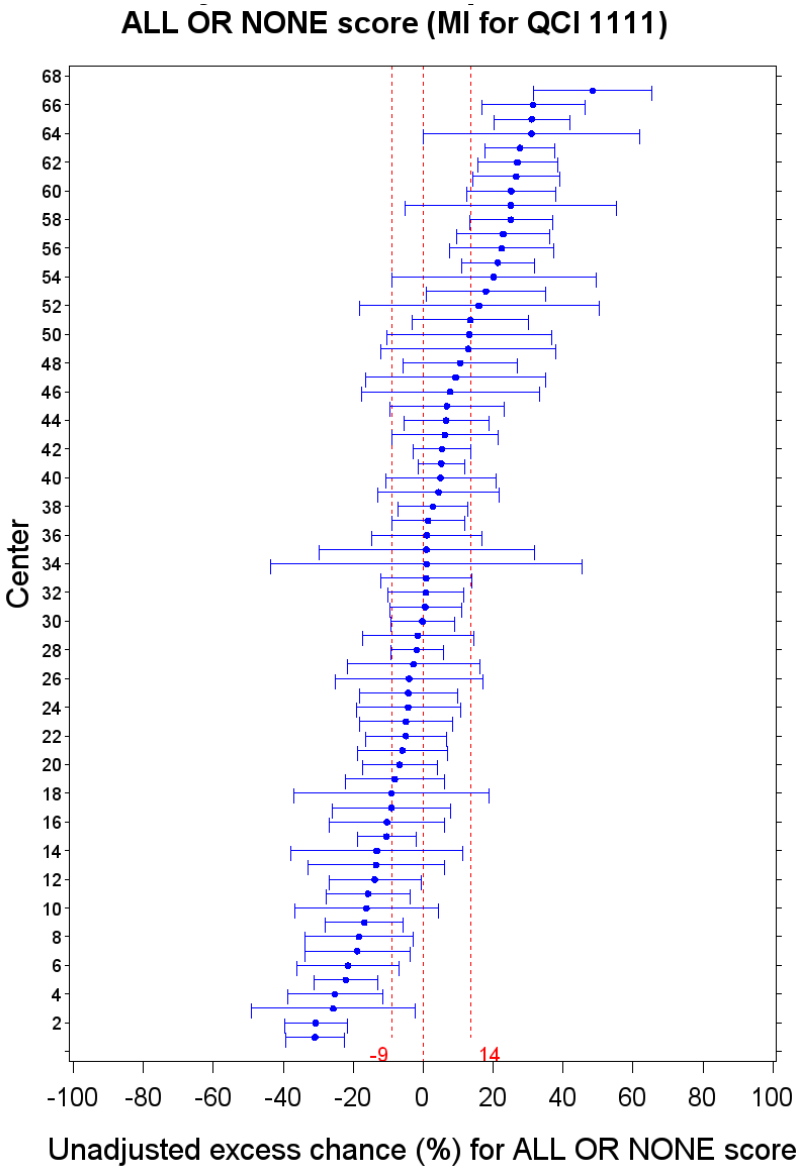


Figure 6: Criteria considered in constructing a combined QI based on "4 selected Process (P) and 3 selected outcome (O) QCIS" of rectal cancer, split by data quality, concurrent validity (PCA), clinical importance and discriminating ability

					Clinical importance			Discriminating ability			
QCI	Short name	Type	Domain	N patients	Survey	Predicitive ability	PROCARE consensus	Visually	% only 0/1	IQR	Random effects variance
1111	*OS*	O	1	3103	5		1		7	14%	
1217	*Time_histo-1ther*	P	2	2687	2.5	0.9467	2				0.0001
1231	*%R0res*	O	4	2914	5	0.0001	1	2	16	11%	0.0001
1232a	*%Defin_ostomy*	P	4	2945		0.0001	1	1	3	19%	0.0001
1234b	*%Major_morb*	O	4	2913	3	0.0001	2	3	26	6%	0.0319
1273	*%Dist_Margin_Rep*	P	8	2051	4.5	0.0012		1	23	17%	0.0001
1274	*#Nodes_Examined*	P	8	2714	5	0.0027	1				0.0001

Survey results are median scores over all responses; PROCARE consensus results are: 1: highly relevant, 2, secondary order, 3: not relevant;Visual discriminating ability is scored as: 1: good,

7.2 CALCULATING SCORES BASED ON A BINARY QI FOR QCIS 1111, 1273, 1274, 1231, 1211 AND 1272

The all-or-none scores for the composite QI is based on the probability to survive 3 years or longer (QCI 1111) and 5 other binary quality criteria (defined previously for QCI's 1273,1274, 1231, 1211 and 1272). To obtain a binary index -for (not) having survived longer than 3 years- one needs to estimate the 3-year survival probability in patients who did not have follow-up for at least 3 years. To this end, a Cox proportional hazard model is used which is built in a forward stepwise manner as done previously for domain 1 aggregation (see section 2).
We calculate the scores based on the aggregated binary indices. For the survival index one uses an imputation procedure. The procedure is repeated 10 times to obtain averaged estimates of the excess center-specific probabilities.

7.3 ADJUSTMENT WITH MAIN EFFECTS:

One needs to ajust the logistic regression model for each imputed score outcome.

7.3.1 Main effects based on "imputed" score 1

The most significant factor in a model corrected for confounding by age and gender is ASA ($p<0.0001$). Next in order, the factors level ($p<0.0001$), cStage ($p=0.026$), cT4 ($p=0.014$) and surgery ($p=0.045$) enter the model. No other factors enter the model (smallest p-value is 0.29).

7.3.2 Main effects based on "imputed" score 2

The most significant factor in a model corrected for confounding by age and gender is ASA ($p<0.0001$). Next in order, one enters the factors level ($p<0.0001$), cStage ($p=0.0006$), cT4 ($p=0.018$; 2^{nd} in order to the most significant factor mode of surgery with $p=0.010$, but chosen to parallel the previous adjustment) and surgery ($p=0.0018$) enter the model. No other factors enter the model (smallest p-value is 0.06).

7.3.3 Main effects based on "imputed" score 3

The most significant factor in a model corrected for confounding by age and gender is ASA ($p<0.0001$). Next in order, one enters the factors level ($p<0.0001$), cStage ($p=0.0044$), cT4 ($p=0.018$) and surgery ($p=0.06$; 2^{nd} in order to the most significant factor mode of surgery with $p=0.035$, but chosen to parallel the previous adjustment) enter the model. No other factors enter the model (smallest p-value is 0.12).
Here we decide to take identical adjustments with main effects ASA, level, cStage, cT4 and surgery. One notes that mode-of-surgery could have been used as a valid alternative to surgery (in models with all-or-none scores "2" and "3").

7.4 INTERACTIONS BETWEEN MAIN EFFECTS

Subsequently, interactions are added to the model with main effects for age (with a different slope before and after the breakpoint of 70 years), ASA, level, cStage, cT4 and surgery.

Table 9: Candidate Interactions for the composite model

age [cont] -ASA score [ref=I]
age [cont] -cSTAGE[ref=I]
age [cont] -cT4[ref=No]
age [cont] -gender [ref=Male]
age [cont] -Surgery[ref=PME]
age [cont] -Tumour Level[ref=Low]
ASA score [ref=I] -cSTAGE[ref=I]
ASA score [ref=I] -cT4[ref=No]
ASA score [ref=I] -gender [ref=Male]
ASA score [ref=I] -Surgery[ref=PME]
ASA score [ref=I] -Tumour Level[ref=Low]
cSTAGE[ref=I] -cT4[ref=No]
cSTAGE[ref=I] -gender [ref=Male]
cSTAGE[ref=I] -Surgery[ref=PME]
cSTAGE[ref=I] -Tumour Level[ref=Low]
cT4[ref=No] -gender [ref=Male]
cT4[ref=No] -Surgery[ref=PME]
cT4[ref=No] -Tumour Level[ref=Low]
gender [ref=Male] -Surgery[ref=PME]
gender [ref=Male] -Tumour Level[ref=Low]
Surgery[ref=PME] -Tumour Level[ref=Low]

Now we add interaction terms starting from the most significant interaction “cStage by surgery” (p=0.0070). Some interaction effects could not be estimated, i.c. cstageII by cT4 missing, cstageXM by cT4 (level “ Yes”), cstageXM by cT4_missing, Asa missing by all cstage levels (II, III, IV and missing levels).

No further interactions are found to contribute significantly (smallest p-value is 0.15).

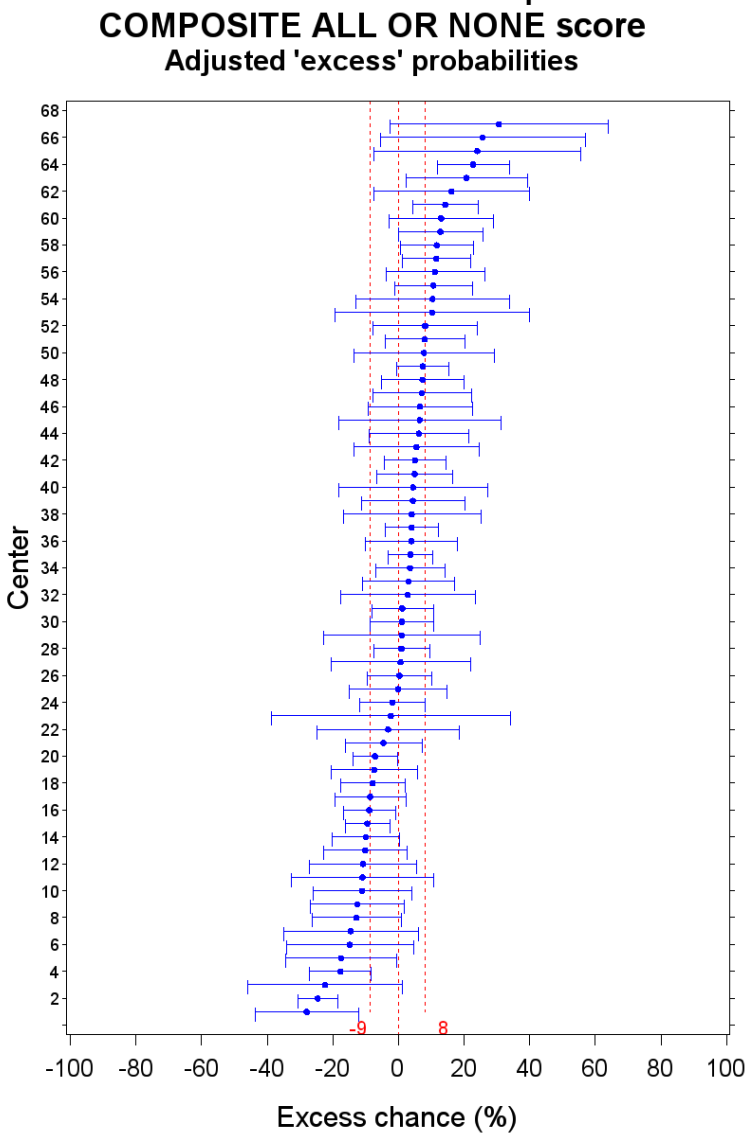
Hence, our final model adjusts for age (with a different slope before and after the breakpoint of 70 years), gender, ASA score, Tumour level, cStage, cT4, surgery and “cStage by Surgery”.

We will apply the adjustments determined here to predict all-or-none scores “1” (first imputed score dataset) also to the other score dataset, i.e. one calculates the adjusted centre-specific excess probabilities based on an average of 10 “imputed” score models.

7.5 "COMPOSITE" ALL-OR-NONE SCORE

A first assessment of the discriminating ability between centers of this adjusted "all-or-none" score is made by examining the caterpillar plot of excess probability in Figure 7. In this caterpillar plot we see 2 centers performing 'significantly' below P25 (-9%) and 1 above P75 (8%).

Figure 7: Caterpillar plot of the adjusted center-specific 'excess' probabilities for the "all-or-none" composite score



8 OUTCOME SCORE AGGREGATION

8.1 CALCULATING SCORES BASED ON A BINARY QI FOR QCIS 1111, 1231, 1234B

The all-or-none scores for the OUTCOME QI is based on the probability to survive 3 years or longer (QCI 1111) and 2 other binary quality criteria (defined previously for QCI's 1231 and 1234b). To obtain a binary index -for (not) having survived longer than 3 years- one needs to estimate the 3-year survival probability in patients who did not have follow-up for at least 3 years. To this end, a Cox proportional hazard model is used which is built as done previously for outcome aggregation (see deliverable 6).

We calculate the scores based on the aggregated binary indices. For the survival index one uses an imputation procedure. The procedure is repeated 10 times to obtain averaged estimates of the excess center-specific probabilities.

8.2 ADJUSTMENT WITH MAIN EFFECTS:

One needs to adjust the logistic regression model for each imputed score outcome.

8.2.1 Main effects based on "imputed" score 1

The most significant factor in a model corrected for confounding by age and gender is cStage ($p<0.0001$). Next in order, the factors ASA ($p<0.0001$), cT4 ($p<0.0001$), and Mode of Surgery ($p=0.00014$) enter the model. No other factors enter the model (smallest p-value is 0.29).

Here we decide to take identical adjustments with main effects cStage, ASA, cT4 and Mode of surgery.

8.3 INTERACTIONS BETWEEN MAIN EFFECTS

Subsequently, interactions are added to the model with main effects for age (with a different slope before and after the breakpoint of 70 years), cStage, ASA, cT4 and Mode of surgery.

Table 10: Candidate Interactions for the composite model

age[cont.] - ASA[ref=I]
age[cont.] - cStage[ref=I]
age[cont.] - cT4[ref=No]
age[cont.] - gender[ref=male]
age[cont.] - modeofsurgery[ref=Sched.]
ASA[ref=I] - cStage[ref=I]
ASA[ref=I] - cT4[ref=No]
ASA[ref=I] - gender[ref=male]
ASA[ref=I] - modeofsurgery[ref=Sched.]
cStage[ref=I] - cT4[ref=No]
cStage[ref=I] - gender[ref=male]
cStage[ref=I] - modeofsurgery[ref=Sched.]
cT4[ref=No] - gender[ref=male]
cT4[ref=No] - modeofsurgery[ref=Sched.]
gender[ref=male] - modeofsurgery[ref=Sched.]

Now we add interaction terms starting from the most significant interaction “age by ASA” (p=0.022). Next,. “cStage by Mode-of-surgery” enters the model. Some interaction effects could not be estimated, i.c. ASA missing by all cstage levels (II, III, IV and missing levels).

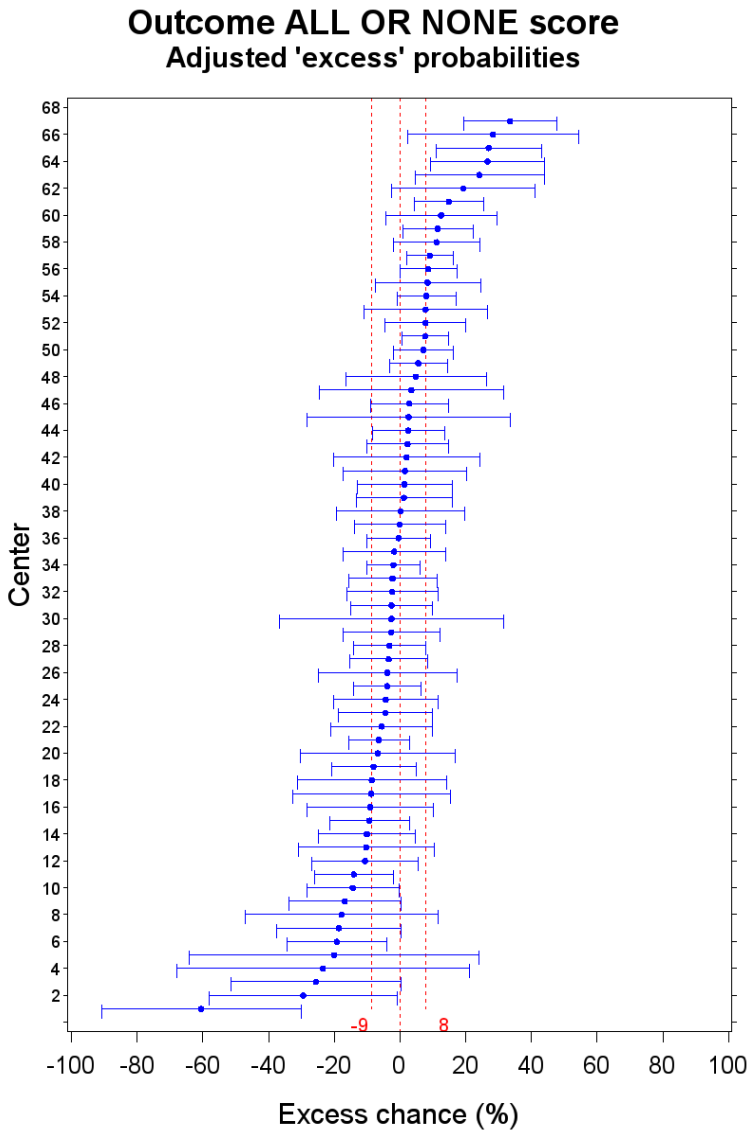
No further interactions are found to contribute significantly (smallest p-value is 0.060).

Hence, our final model adjusts for age (with a different slope before and after the breakpoint of 70 years), gender, cStage, ASA score, cT4, Mode of surgery and “Age by ASA” and “cStage by Mode-of-Surgery”.

We will apply the adjustments determined here to predict all-or-none scores “1” (first imputed score dataset) also to the other score dataset, i.e. one calculates the adjusted centre-specific excess probabilities based on an average of 10 “imputed” score models.

8.4 ADJUSTED “OUTCOME” ALL-OR-NONE SCORE

A first assessment of the discriminating ability between centers of this adjusted “all-or-none” score is made by examining the caterpillar plot of excess probability in Figure 7. In this caterpillar plot we see 1 center performing ‘significantly’ below P25 (-9%) and 3 above P75 (8%).


Outcome ALL OR NONE score
Adjusted 'excess' probabilities
Center
68
66
64
62
60
58
56
54
52
50
48
46
44
42
40
38
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
-9
8
-100
-80
-60
-40
-20
0
20
40
60
80
100
Excess chance (%)

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